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EDITORIAL

Tranquilization*

Many psychologic disorders
are made worse rather than better
by administering tranquilizers

JAMES M. NORTHINGTON, M.D., *Editor-in-Chief*

Paradoxically, an anxious patient may become more anxious because he no longer feels anxious while taking a tranquilizer. He worries because of his lack of worry. In short, natural anxiety may be a normal defense mechanism and therefore may have virtue in its own right. When anxiety is suddenly and completely removed by the administration of a tranquilizing agent, the patient may find himself confused by a situation with which he cannot cope. He, therefore, must substitute a more normal defense mechanism if he can summon one, or break down.

Hostile patients who are filled with chronic anger do not do well on tranquilizers, nor do patients dominated by obsessional mechanisms. Sudden depersonalization may induce a fear of going mad. Latent homosexuals occasionally become active or even hyperactive in an overt manner after the ingestion of tranquilizers.

Equanimity, tranquillity and peace of mind are found in oneself and not in a bottle on the pharmacist's shelf. It may be true that our civilization is bungling through a period of idealogical controversy, but every civilization in human history has floundered from one crisis to another. If crisis produces tension (or *vice versa*), then this tension should be used construc-

*An article by C. C. Shaw and P. W. Felts in the *American Journal of Medical Sciences*, 237:141-149, 1959, expressed the thoughts summarized in this editorial and in some instances implemented by those of the author. J.M.N.

tively to overcome the crisis so that the drive to self-transcendency may become a positive force for good.

Anxiety is like smoke which precedes fire. The fire may be used to great advantage in our daily lives as a source of energy. If it rages out of control, a conflagration ensues. Tranquilizers may be used judiciously to prevent or put out smouldering brush fires, but they should not be called upon to quench a forest fire. Neither should they be employed to completely stifle anxiety from which the warm, blue flame of ambition and accomplishment is lit.

Peace of mind, like the pursuit of happiness, is a transitory affair. It is not an end in itself. It should be sought primarily as a means to insure our ability to live and to keep on living, to face the present and the future with enthusiasm and not to mourn the past.

In 1663, the great poet, John Milton, wrote: "The mind is its own place and in itself can make a Heaven of Hell, a Hell of Heaven."◄

Doctors, the Public, and Acceptance of Scientific Advances

Conflicts in the press or on the public stage on acceptance of health measures have been made through the ages. We can remember the slow acceptance of chlorination of public water supplies, the course of various anti-vivisection bills in State legislatures, tirades against the pasteurization of milk, the use of aluminum in cooking utensils, and controversies over fluoridation of water supplies still go on.

The Salk vaccine was widely and promptly accepted, perhaps because it protected against a crippling and tragic disease which hit quickly, against which there were no defenses. Or was it because in recent years the public had learned a great deal about polio? At least one group opposed the Salk vaccine. Many of the people who were in that anti-polio vaccine campaign are fighting fluoridation now. In the Nation-wide polio vaccine trials the people were informed about the problem, were told what questions needed to be answered, why it was important to get answers to these questions, and what could be expected if the answers were favorable. With such a background, coupled with the great interest that had been around through the fund raising activities of the National Foundation for Infantile Paralysis, thousands of U.S. parents were willing [even eager] that their children be inoculated with an experimental vaccine. A good many were willing to join controlled experiments in which they did not know if their children were or were not being protected. Adults and children thereby learned something about the scientific method. The public is now eager to accept the measures which science and technology offer.

Doctors probably are the only persons with considerable scientific background with whom most people ever have direct personal contact. It is suggested that they not only play the traditional role as protector of the family health, but that they assume an additional role as interpreters of science and its methods.

Baumgartner, L., *Bull. New York Acad. Med.*, 34: 609-613, 1958.

ORIGINAL ARTICLE

Bronchogenic Carcinoma: Etiologic Considerations

Although tobacco is an alleged carcinogen, the increased incidence of lung cancer is more indicative of improved diagnostic techniques and longevity

MILTON B. ROSENBLATT, M.D.,* *New York, New York*

The marked rise in the incidence of lung cancer has presented many problems. In the United States, bronchogenic carcinoma now accounts for 10 per cent of the total cancer deaths, more than 20 per cent of the cancer deaths among men between 45 and 70 years. Similar increases have been noted in other countries. In England and Wales, the crude death rate from lung cancer increased from 8 per million in 1900 to 321 per million in 1952. Explanations for the increased prevalence have included the following etiologic possibilities:

1. Inhalent carcinogens from automobile exhausts and industrial combustion motors.
2. Tarring of roads.
3. Inflammatory metaplasia from antecedent bronchopulmonary infection.
4. Occupational exposure to asbestos, silica and chromium.
5. Smoking.

In general, the inhalation theories have not stood the test of time. Reluctance to acknowledge air pollution as an important factor was based on the universal exposure of the population to gaseous irritants and the lack of correlation with the incidence of the disease as well as the sex and age distribution. The carcinogenic action of tar led to the implication of tarring of

*Associate Professor of Medicine, New York Medical College; Visiting Physician, Metropolitan Hospital; Co-author of "Cancer of the Lung," Oxford University Press, 1956.

the roads but this was refuted by studies showing that the increased incidence preceded tarring of roads[1] and that it had occurred in areas in which neither tarring nor automobiles had made any impact.[2]

The occurrence of metaplasia in the bronchial mucosa as a sequel to bronchopulmonary inflammatory disease led to consideration of a relationship between the influenza epidemic of 1918-1919 and the subsequent increase in bronchogenic carcinoma.[3] Similarities between post-inflammatory squamous metaplasia and malignant changes have been often noted and allusions made as to the former representing a possible pre-cancerous condition. It is difficult to establish a causal relationship between the two occurrences, because the early symptoms of bronchogenic carcinoma are often due to infection distal to the bronchial obstruction. The first clinical manifestations of the disease may present themselves as syndromes indistinguishable from lobar pneumonia, segmental pneumonitis, abscess or bronchiectasis. Specific infections such as tuberculosis and fungus disease have also been implicated on the basis of co-existence.

Exposure to silica and asbestos has been considered of etiological importance in instances in which both pneumonoconiosis and cancer were present.[4] The irritant effect of chromium on mucous membranes and its wide industrial use led to consideration of a possible carcinogenic effect.[5] However, the argument for occupational exposure is not a strong one. The total number of reports of lung cancer cases presumably related to specific industrial exposure is too small to merit any serious consideration. Some years ago interest was aroused by the high incidence of lung cancer in the workers of the *Schneeberg (Germany) and Joachimstal (Czechoslavakia) mines.* Chronic radon exposure was considered the offending agent but later studies cast doubt on the conclusions in favor of hereditary considerations based on the inbreeding that had occurred for centuries in the mining localities.[6] In studying occupational exposure in hospitalized patients with lung cancer it has been found that the occupations are usually a reflection of the general status of the hospital population.[7]

In recent years major interest has centered on the carcinogenic role of tobacco. In the early part of the 20th century the onus was placed on cigar and pipe smoking; now the emphasis is on cigarettes. The marked rise in cigarette consumption in the United States tended to corroborate the conclusions of the statistical studies sponsored by the American Cancer Society and by public health agencies abroad. There has been a general unanimity among the investigators that cigarette smoking is statistically related to lung cancer and that the mortality ratio of the heavy smoker for lung cancer is far greater than that of the non-smoker.[9-16] In corroboration of the statistical data, there has also been presented some experimental evidence purporting to show the

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14. Wynder, E., & Graham, E., *J.A.M.A.*, 143:329, 1950.
15. Watson, W., & Conte, A., *Cancer*, 7:245,1954.
16. Korteweg, R., *Cancer*, 9:163,1953.

carcinogenic effect of tobacco on the skin of mice.[17]

During the recent Congressional investigation on cigarette filters in Washington, many dissenting opinions were expressed in regard to the potentialities of smoking as a cause of lung cancer. These objections may be summarized as follows:

1. Cancer of the lung has been an established entity in the medical literature for 150 years, antedating the era of cigarette smoking by a century.[18-20]

2. In institutions with routine autopsies and awareness of the disease there has been no real increase in the ratio of lung cancer to total cancers.[21-25]

3. The current difficulties in the diagnosis of bronchogenic carcinoma suggest that a percentage of the huge respiratory death rate in the early part of this century may well have been due to lung cancer. If this diagnostic error is estimated as low as 5 per cent, the death rate from lung cancer at the turn of the century would have been as great as it is today.

4. The validity of the statistical conclusions has been challenged on the basis of improper selection of controls, lack of autopsy confirmation of the cause of death, and lack of correlation between the death rates of the heavy smokers in the survey as compared with the death rates for the total white male population in the United States.[26]

5. The relationship between induction of skin cancer in susceptible strains of mice and bronchogenic carcinoma remains to be established. Experienced investigators have found tobacco tar condensate to be a very weak carcinogenic agent in comparison with many other substances.[27] The perpetual tobacco staining of fingers of heavy smokers have produced no increase in the incidence of cancer of the skin. The experimental exposure of mice to tobacco smoke for long periods of time did not produce lung cancer.[28] Bronchogenic carcinoma has never been produced in the experimental animal by the use of tobacco or tobacco products.

Before the statistical evidence can be accepted as establishing a causal relationship between smoking and lung cancer, it must be determined whether the rise in incidence is real or apparent. There is considerable evidence that the epidemic-like increase is due to factors totally unrelated to cigarette consumption. These factors are the development of better diagnostic facilities and longevity of the population.

Those who have been working in the field of pulmonary diseases for many years are well aware of the lack of interest in lung cancer and the paucity of diagnostic facilities during the first quarter of this century. In some institutions, bronchogenic carcinoma was considered a rare disease despite the abundance of reports in

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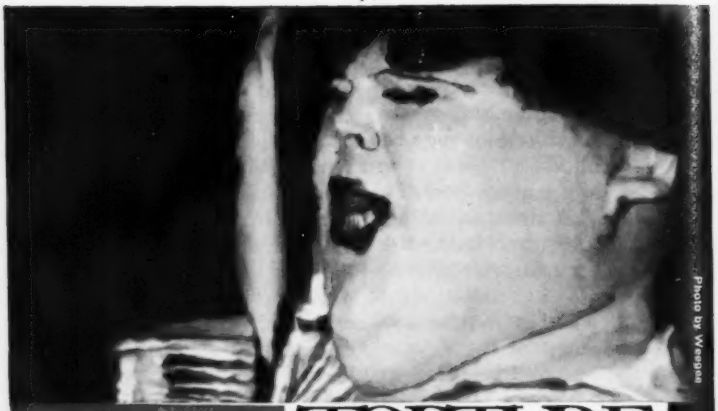

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both the American and European medical literature. The routine use of diagnostic roentgenology and its special techniques represent a development of the last 25 years. Exfoliative cytology has been utilized in most hospitals for less than 15 years. Bronchoscopy was formerly done on rare occasions and is now a routine diagnostic procedure in all pulmonary problems. One famous pulmonary hospital reported 6 bronchoscopic examinations annually prior to 1930, and over 800 annually 25 years later.[29] Exploratory thoracotomy, formerly a last resort, is now performed extensively throughout the country. It would, indeed, be a sad reflection if this greater availability of diagnostic tools did not result in the recognition of a greater number of cases.

It has been repeatedly pointed out that whenever an inaccessible cancer becomes accessible, the incidence automatically increases. The incidence of cancer of the larynx and nasopharynx have changed little in recent years, because the methods of diagnosing these conditions has remained virtually unchanged for decades.[30-31] Cancers of the skin, cervix and breast have shown no remarkable changes in incidence. In 1924, the national death rate for lung cancer was stated as 1.5 per 100,000, whereas in San Francisco, where a survey of lung cancer was taking place, the death rate was over 6 per 100,000. A public health survey once attributed the high incidence in Philadelphia to the diagnostic facilities of the Jackson Bronchoscopic Clinic. As early as 1896, the clinical manifestations of bronchogenic carcinoma were described in great detail and the rising incidence was viewed with alarm.[32]

The techniques utilized in the study of pulmonary diseases in recent decades have yielded a far greater return than an increase in lung cancer cases. Conditions formerly considered as tuberculosis, unresolved pneumonia or non-specific inflammatory disease have since been correctly diagnosed as fungus infections, cystic disease, pulmonary infarctions and benign tumors. Bronchial adenoma showed a tenfold increase in incidence between 1940 and 1950.[33] There is no question that the reason for this increase was improved diagnostic facilities. Inasmuch as bronchial adenoma arises from the submucous glands rather than from the epithelial surface, the increased incidence could not possibly have resulted from exposure to inhalent carcinogens.

The second factor responsible for the increased incidence of lung cancer is longevity. Bronchogenic carcinoma is a disease of late adult life, the majority of cases occurring in the 5th, 6th and 7th decades. Few cases have been reported in patients under 40 years of age. The average life span of the population has increased steadily and is now 68 years. In the first decade of this century there were 4,000,000 people living past the age of 65, today the number in this group exceeds 14,000,000. There are also 33,000,000 adults between 45 and 64 years.[34] More susceptible people are reaching the cancer age.

As the average length of life increases it is to be expected that there will occur a greater number of cases of lung cancer, as well as of other

29. Smithers, D., *Brit. M.J.*, 2:1235,1953.
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cancers. The incidence of lung cancer showed a greater rise in recent years because of the progress in diagnosis. Current public health statistics show that the rate of increase of lung cancer is slowing.[35]

Some reports give the ratio of lung cancer between men and women as 10:1. A recent national report states that there are 26,000,000 men in this country who are regular cigarette smokers, and 15,000,000 women who are regular smokers. If smoking were a factor in lung cancer, the marked difference in sex distribution should be gradually declining, but the opposite has occurred. Although more lung cancers are being diagnosed in females, the ratio has actually increased.

The greater susceptibility of the male is, in all probability, due to basic sexual factors, comparable to the occurrence of more breast cancers in women. Few women who are susceptible to cancer reach the age at which lung cancer is found.

The increase in lung cancer has not been confined to England and the United States but has occurred throughout the world, in countries with wide variations in habits, occupations, and climate. There has been no universal correlation observed between amount of tobacco consumed and incidence of lung cancer. The increase has occurred in countries where the cigarette consumption has been fairly stationary, such as Germany, Austria and Turkey, as well as in countries with a marked rise in cigarette consumption, such as the United States, Italy, and Canada.[36]

35. Dorn, H. F., *Indust. Med and Surgery*, 23:61, 1954.
36. U.N. Food and Agr. Org.: Tobacco, Commodity Series Bull. No. 20, October, 1952.
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Between the years 1938 and 1949, deaths from lung cancer increased 200 per cent in Canada, Denmark and Finland, 100 per cent in Austria, Italy, Norway, Ireland, the Netherlands, New Zealand, and the European population of the Union of South Africa. Although lung cancer is reported as a rarity in some areas, the establishment of diagnostic centers soon discloses an increased incidence. A study at the Peiping Union Medical College revealed 16 cases diagnosed histologically between 1936 and 1940, half of the cases during the last year of the survey.[37] In an area of East Pakistan conspicuously free of tarred roads, automobiles and cigarette smokers, the establishment of a diagnostic service was followed by the discovery of 20 cases of bronchogenic carcinoma in a period of 18 months.[38]

It is more reasonable to attribute the increased incidence of lung cancer to such universally applicable factors as improved diagnostic methods and increased life span, than to place the onus on alleged carcinogens in tobacco or polluted air. The evidence against tobacco is still largely statistical and consists of a relationship between two variables, tobacco and lung cancer. This is insufficient to establish a cause-and-effect relationship. The same studies showed an increased mortality ratio for cirrhosis of the liver, coronary artery disease, peptic ulcer, non-cancerous pulmonary disease and non-pulmonary neoplasms.

SUMMARY

1. The increased incidence of lung cancer has resulted in much speculation as to etiology.

37. Hsieh, C. K., et al., *Chinese M.J.*, 58:381,1940.
38. Ibrahim, M., *Dis. Chest*, 26:286,1954.

2. Air pollution, inflammatory metaplasia, and occupational exposure have been named as carcinogenic agents, but major interest has centered on cigarette smoking.
3. Statistical studies, both here and abroad, have been presented as evidence of a causal relationship between lung cancer and cigarettes.
4. Failure to experimentally produce bronchogenic carcinoma with tobacco products and lack of general acceptance of the statistical surveys call for further study of this question.
5. Lung cancer had been recognized for more than a century before cigarette smoking became popular.
6. In institutions familiar with the disease, the ratio of lung cancer to total cancers was practically the same in the 19th century that it is now.
7. The great advances in diagnostic progress make impossible comparison of statistical incidence now with that of a quarter of a century ago.
8. Lung cancer is a disease of late adult life and the increased life span of the population has resulted in more people reaching the cancer age.
9. The predominance of lung cancer in men has suggested a relationship with smoking, but the last three decades have witnessed a tremendous increase in women smokers without a corresponding increase in the death rate from lung cancer among women.
10. The wide geographical distribution of the increased incidence is more indicative of improved diagnosis and longevity than of increased exposure to alleged carcinogens.◀

ORIGINAL ARTICLE

Ulcerations of the Feet and Toes

A discussion of the various causes and treatments of ulcerations of the feet and toes is here presented

EGMONT J. ORBACH, M.D., F.I.C.S., F.A.C.A.,
New Britain, Connecticut

Ulcerations of the terminal parts of the lower extremities often present diagnostic and therapeutic problems. Infections, disturbance of the circulation (arterial, venous and lymph systems), diseases of the spinal cord and peripheral nerves, blood dyscrasias, malignant tumors, and avitaminosis may be causative.

The following causes should be considered:

1. Vasospastic diseases: Raynaud's disease, scleroderma, acrocyanosis, frostbite, trench foot, immersion foot, pernio.

2. Occlusive arterial diseases: Thrombangitis obliterans, arteriosclerosis obliterans, diabetes mellitus, ulcerations occurring after arterial embolism.

3. Ulcerations due to venous hypertension.

4. Ulcerations on the basis of disturbance of the lymph circulation (Lymphedema).

5. Ulcerations on the basis of diseases of the central nervous system and of the peripheral nerves: Syringomyelia, poliomyelitis, tabes dorsalis, neurotrophic ulcerations of the metatarsal regions and toes in diabetes.

6. Unspecific and specific infections.

7. Decubitus ulcers below callous formations and those produced by ingrown toenails.

8. Ulcerations resulting from carcinoma, sarcoma, melanoma, Kaposi sarcoma.

9. Ulcerations on the basis of avitaminosis.

10. Ulcerations on the basis of blood dyscrasias.

Only the more frequently occurring ulcerations will be discussed. This list may be used as a differential diagnostic aide.

MOST ATTENTION TO THOSE COMMONLY SEEN

Most ulcerations of the feet and toes are caused by occlusive arterial disease. The ulcerations are located at the terminating phalanges of toes, over hammertoes, bunions and heels. Occasionally they are found at the interfaces between toes, caused by pressure of one toe against the other.

The ulceration may start as a bulla, which leaves a torpid wound after removal. It may be covered by a leathery black gangrenous skin, especially at the heel and over exostoses. It may be several centimeters in diameter or of minute size, forming the end of a fistula leading to bone and joint space. If near the distal part of the terminal phalanx—under the nail—the bone is early involved, laid open and necrotic. The nails slough off.

The bacterial flora consists of streptococci, staphylococci, coli and other saprophytes. Attention has been called to mycotic infection in gangrene of the lower extremities.[1]

It is difficult to determine the site of the arterial obstruction from the appearance of the ulcerations, whether it is segmentary, diffuse, in the larger arteries or in the arterioli.

1. Samuels, S. S., *New York J. Med.*, 48:1157,1948.

SYMPTOMS AND SIGNS

The patients, usually elderly, complain of intermittent claudication, cold feet and nocturnal rest pain. Plantar blanching appears on elevation, and cyanotic rubor of the feet and toes appears on dependency. Usually the pulse of the dorsalis pedis, of the posterior tibial artery and of the popliteal artery is not palpable. If the obstruction is in the iliac arteries or in the aorta, there will be either a weak femoral pulse or none. In an unilaterally missing pulse the iliac artery on the same side is obstructed; in a bilaterally missing femoral pulse the terminal aorta above the branching of both iliacae communes, or both iliac arteries are occluded. An oscillographic zero-reading above the ankles is a grave sign, although the ulceration may heal spontaneously in a case showing this reading.

SPECIAL CARE IN DIABETES

The diabetic is prone to infection, so that a severe cellulitis may spread from the ulcerations. The danger of ascending wet gangrene and sepsis is great, although generally the major arterial circulation is not badly impaired. The toes may be warm and peripheral pulse may be present. The arterioli may be segmentarily occluded, and the spreading infection is the leading symptom. Using antibiotics and adequate incisions in order to open the purulent fascial spaces will, in the majority of cases, save the limb. Packing the spaces with gauze saturated with Azochloramid in triacetin has been advised.[2,3]

2. Samuels, S. S., *Surg. Gynec. & Obst.*, 69:342,1939.
3. Samuels, S. S., Diagnosis and Treatment of Vascular Diseases, The Williams & Wilkins Co., Baltimore, pp. 315-319, 1956.

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COLLATERAL CIRCULATION—SIZE OF ARTERY OBSTRUCTED

The more collaterals present, the better the chances for healing. A recent arterial obstruction of a larger artery followed by ulcerations in the area of the foot or toes has a grave prognosis.

FIRST REST—LATER EXERCISE

In the beginning rest is essential, with the leg in light dependency. Later on, active motions like Buerger's exercises and graded walking exercises may prove helpful, since active motion promotes blood perfusion and formation of collateral vessels. However, this has to be done under close supervision and only within the tolerance of the patient. Signs of cellulitis around the ulcer contraindicate mobilization. The ulceration should be carefully debrided. Boric acid ointment and foot soaks, both of which produce maceration of necrotic tissue, have been used. The necrotic tissue can be removed by excision within the limits of demarcation.[3]

SPECIAL TOPICAL APPLICATIONS

Tryptar and Varidase have been used as topical solution to clean up dirty ulceration with varying success. A powder consisting of powdered blood cells, Tryptar powder and chloramphenicol have proved to be beneficial in healing recalcitrant ulcerations. An ointment containing trypsin and neomycin also has been recommended. Hydrocortisone ointments containing an antibiotic have been beneficial in several cases.

SYMPATHECTOMY RARELY INDICATED

Although sympathectomy in occlusive arterial disease has been widely used, it still remains highly controversial and has a one to three per cent mortality.[4] It is questionable whether a necessary amputation can be carried out at a lower level. It is not recommended for patients over 60 years of age.[5]

Thromboendarteriectomy has been abandoned due to poor results.[4]

OTHER OPERATIVE MEASURES ON TRIAL

Arterial grafts and by-pass operations have been only moderately successful. The number of cases is too small, and the lapse of time too short to allow a conclusive opinion. It is the consensus that these operations are still in the experimental stage.[4,5] However, the steps taken are in the right direction, and with improvement of technic and availability of improved material an important therapeutic tool will be available.

Arterial grafts or by-pass operations will be successful only in cases of segmental occlusion, provided the distal artery is patent. These operations will be valueless where there is diffuse arteriosclerosis and endarteritis obliterans. The operative indications will, therefore, be dependent on the interpretation of arteriograms.

ARTERIOGRAMS AND AORTOGRAMS

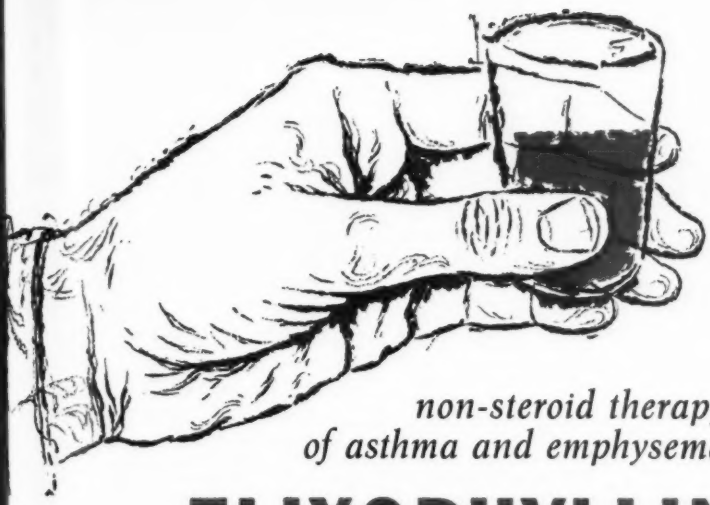
Since arteriograms and especially aortograms are not without danger, the physician should ask himself the following questions before undertaking this procedure.[5]

1. Are the patient's age and general health such that surgical treatment or angiography is justifiable?

2. Are the patient's symptoms of such severity as to warrant surgical treatment?

3. Are there any contraindications (bleeding disorder, current anticoag-

4. Ziffren, S. E., *Angiology*, 8:489-503,1957.
5. Estes, E. J., *Angiology*, 9:114-125,1958.



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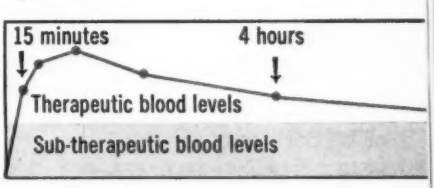
DOSAGE: *First two days:*
45 cc. (*three tbsp.*) on arising;
45 cc. (*three tbsp.*) on retiring;
45 cc. (*three tbsp.*) once midway between above doses (*about 3 P.M.*)



After two days of therapy the size of doses should be slightly decreased.
Each tablespoonful contains: theophylline 80 mg., alcohol 3 cc.
Prescription only – bottles of 16 fl. oz.

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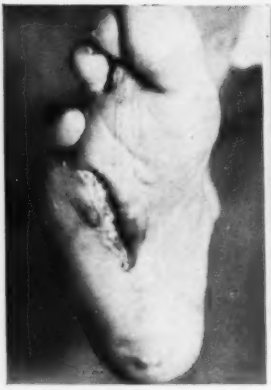
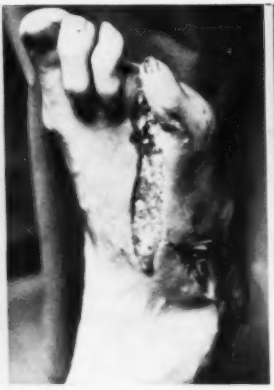




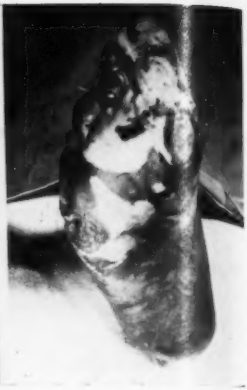


FIGURE 1 FIGURE 2 FIGURE 3

FIGURE 1: Ascending wet gangrene and cellulitis developing after amputation of gangrenous fourth toe. FIGURE 2: Treatment consisted in wide incisions at the dorsum and planta with excision of necrotic tissue, plus diet, insulin, antibiotics. FIGURE 3: Neurotrophic ulcerations of the planta in a patient with diabetes (Kimmelstiel-Wilson disease.)

ulant therapy, sensitivity to the radiopaque substance)?

Without a potential future operation in mind, an angiogram will be of no help to the patient in respect to his health.

GENERAL CONSIDERATIONS

In selecting the patients for grafts and by-passes, one has to consider the status of his general condition. Is he suffering from severe coronary, renal and/or cerebral arteriosclerosis? In this event the patient will probably not die from the sequelae of his peripheral arteriosclerosis, but from either coronary occlusion, uremia or cerebral accident.[5]

EVEN MINOR SURGICAL PROCEDURES PRESENT DANGERS

Minor local operations are in order to stimulate healing, such as scarification of wound edges after the ulcer has been cleaned of necrosis and debris. Occasionally the amputation of a toe that exhibits a necrotic ulcer is justified. However, these minor amputations are not always without inherent dangers, insofar as the operation wound does not heal and an infection may spread from the operation site. The author, therefore, would hesitate to undertake such minor intervention, as the following case exhibits:

A diabetic of 64 was treated for four years for a recurrent toe infection. Each time antibiotics were given. The fourth toe of his right foot became swollen and painful. Bed-rest and foot soaks were advised. The diabetes was mild and controlled with 20 units of protein-zinc insulin. Blood sugar never exceeded 190 mg. per cent. The pulse of the dorsalis pedis was palpable, the oscillometric reading above the ankles was 1½ de-

grees. The origin of the repeated infection was a small fistula at the outer side of the fourth toe. A probe could be passed into the proximal interphalangeal joint. The patient lost 3 to 4 weeks' work several times a year. Amputation of the involved toe was done and the head of the fourth metatarsal head resected. The wound was left partially open, and massive antibiotic therapy with strict diabetic regimen instituted. There developed an ascending infection of the metatarsal region, which required frequent wide incisions and excision of necrotic tissue, including tendons (Fig. 1 and Fig. 2). It took over one year before all wounds were healed. The patient finally lost his job and was pensioned.

The question is still open whether the patient might have suffered an ascending infection, *even without operation.*

THE INDICATIONS FOR MAJOR AMPUTATIONS ARE FEW

Major amputations in the majority of cases can be avoided by treating gangrenous limbs conservatively, using sound surgical principles.[2] Only if the gangrene becomes extensive, the pain and infection uncontrollable, should a major amputation be undertaken.

KIMMELSTIEL-WILSON DISEASE

Occasionally a patient with advanced diabetes develops neuropathic ulceration of the soles and toes. This condition is a partial picture of the retinopathia, nephropathia, neuropathia triad (Kimmelstiel - Wilson disease). The ulceration starts underneath a callus of the sole of the metatarsal region (Fig. 3). Eventually a cellulitis around the ulcer spreading to the forefoot sets in, which may lead to a highly febrile sepsis. If unattended, the patient may succumb. These mal perforants, which should not be confused with mal perforant of tabes dorsalis, show very thick callous edges, with necrotic granulations at the base of the ulcerations. Tendons and bone may be seen at the fundus. The patient walks around with little discomfort. Self-amputation of toes frequently occurs. The ulcers are caused by trophic disturbances due to diabetic involvement of the peripheral nerves. In addition arteriosclerotic obstruction of the arterioli plays a role.

Under careful treatment these ulcerations can be cured, although new ulcers may form. The therapy consists of excision of the callous wound edges and bulky dressings. This can be done without anesthesia. Even toes can be removed without it. The diabetes has to be strictly supervised. In case of ascending cellulitis the patient should be hospitalized. Intensive antibiotic therapy, bedrest and surgical intervention are necessary.

In recurrent cases transmetatarsal amputation has been recommended.

Ulcerations of the feet due to venous hypertension, varicose veins or lymphedema are infrequent. They are usually located in the vicinity of the medial malleolus. Eradication of the veins by either surgery or injections, or both, compression bandages using foam rubber sponges, and ambulation will effect a cure.

Ulcerations due to unspecific microbial and fungal infections are occasionally seen even with intact venous and arterial circulation. They constitute ulcerations on the basis of eczema or contact dermatitis. Antibiotic and fungicidal ointments or powders in conjunction with corticosteroids have been used with good

success. Sensitation should be avoided.

Ulcers caused by specific infections such as lues or tuberculosis are rare.

DECUBITAL ULCERS

There are three types of decubital ulcers:

1. The ulcerations at the heel or over bony prominences in bedridden, paralytic and undernourished seriously ill patients.

2. The ulcerations produced by callosities.

3. The ulcer of the nailbed produced by an ingrown toenail.

Decubital ulcerations of cachectic and paralyzed patients are difficult to heal. High protein diet together with local therapy (blood powder) may be successful. If the vitality of the patient is not too low, surgical closure by flap formation, especially in the trochanteric and sacral region, is possible. Usually the patient will succumb to his underlying illness before the ulcer heals. Prevention is of great importance.

The ulcer beneath a callus will readily heal after removal of the callus. In diabetic patients a mal perforant is often hidden underneath such a callus.

The decubitus ulcer caused by ingrown toenail will heal after removal of the nail. If it returns, a wedge excision of the nail plus nail bed is advised. Occasionally the ingrown toenail syndrome is the cutaneous expression of a serious underlying arterial disease. Therefore, the vascular status of the extremity should be thoroughly investigated before surgery is contemplated, in order to avoid disastrous results.

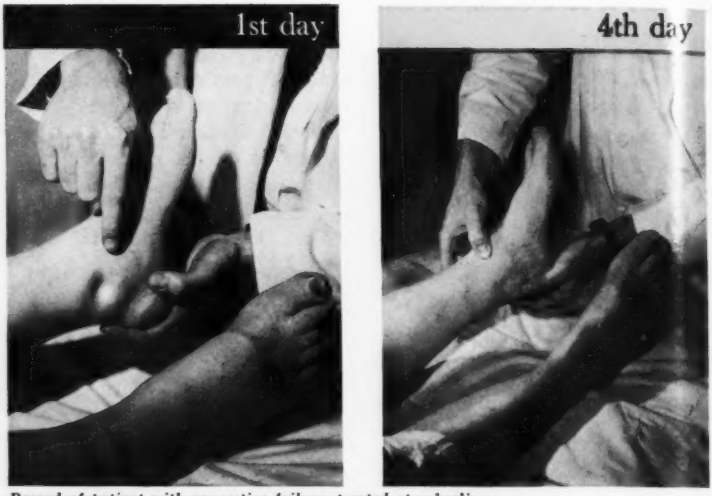
CONCLUSION

Ulceration of the feet and toes may be prevented by careful hygiene of the feet. Daily bath and application of fungicidal powders are advisable for the older group patients, especially if they are affected with diabetes and vascular diseases. Shoes have to be properly fitted, and pressure must be avoided. Cutting of nails has to be done without injuring the skin. The treatment of corns should not be left to the patient, but should be done either by the physician or by a competent chiropodist. Many a limb has been lost due to careless treatment of minor injury of toes and feet. Each break in the skin is a potential road to gangrene.◀

Reducing Gonad Irradiation in Pediatric Diagnosis

There is a growing tendency to resort to radiology in almost every diagnostic problem in pediatrics. When the gonads are outside the direct beam, reduction of cone size causes a reduction of more than four-fifths in the ovary exposure dose. Lead shielding, where practicable, and high-speed intensifying screens are mandatory. Finer detail can be obtained without the screen, which is not needed in most cases for studying the smaller child's moving during the longer exposure. One of the largest factors is the reduction of nondiagnostic and unnecessary radiologic examinations. "Routine" fluoroscopic examinations, those most productive of radiation exposure, are often useless.

Bishop, H. A., et al., *California Med.*, 90:20-25,1959.



Record of patient with congestive failure, treated at a leading Philadelphia hospital. Photos used with permission of the patient.

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ORIGINAL ARTICLE

d-Chlorpheniramine in Allergy

The antihistaminic activity of the stereoisomers of chlorpheniramine resides essentially in the dextrorotatory form

GEORGE BABCOCK, JR., M.D., *Bloomfield, New Jersey,* and
LOUIS A. PACKARD, M.D., *Prescott, Arizona*

INTRODUCTION

Stereoisomerism—the ability of certain compounds to rotate the plane of polarized light—is a physical phenomenon with occasionally significant therapeutic implications. Whether or not an organic compound includes this potential optical activity can be predicted from its structure: possession of a carbon atom to which are attached four different atoms or radicals. Theoretically these compounds are separable into "mirror images" which, although identical chemically and physically, usually differ in their pharmacologic properties. In many drugs characterized by this asymmetric structure (amphetamine for example) the major pharmacologic activity occurs in one rather than in both of the stereoisomers.

Few antihistamines are of such structure as to permit separation. However, the racemic form of chlorpheniramine maleate* contains an asymmetric organic molecule which enabled the compound to be separated into its stereoisomers.[1] A marked difference in the pharmacologic effect of the dextrorotatory and levorotatory forms was noted. The *d*-stereoisomer

**Chlor-Trimeton®*, Schering Corporation, Bloomfield, New Jersey.

1. Walter, L. A., & Kennedy, C., Report to the Schering Corporation, 1958.

is the component of predominant antihistaminic activity.

PHARMACOLOGY

The pharmacology of racemic chlorpheniramine maleate was described by Labelle and Tislow,[2] who tested this compound in guinea pigs for its ability to protect against lethal intravenous doses of histamine and in mice for its toxicity. The potency and also the therapeutic index (LD_{50} divided by ED_{50}) was higher than that of any other antihistamine tested. This agent was shown to have a notably low acute and chronic toxicity index systemically and locally.

Parallel studies on *d*-chlorpheniramine maleate* were conducted in guinea pigs.[3] Its oral antihistaminic activity proved to be at least twice that of the racemic compound. The potency ratio of the dextrorotatory to the racemic and to the levorotatory forms is on the order of 100:50:1. These authors[3] also noted that it acted similarly to chlorpheniramine maleate in the dog, but that the antihistaminic effect of the former was considerably more marked.

Oral subacute toxicity studies with *d*-chlorpheniramine were performed in the monkey and in the rat and revealed no deleterious effect on general deportment, body weight, hemograms, blood chemistry, hepatic bromsulphalein clearance, term organic weights, or gross pathology at necropsy.[4]

Since *in vivo* studies showed that the toxicity, on a weight-for-weight basis, was the same for *d*-chlorpheniramine and racemic chlorpheniramine maleate but considerably higher for the therapeutically inactive *l*-stereoisomer, it was concluded that in the human the former, on a weight-for-weight basis, would prove to be twice as potent, but no more toxic, than its older analogue. It was shown to have a therapeutic index of 3,380, the highest thus far reported for any antihistamine.

CLINICAL BACKGROUND

Antihistamines antagonize many of the characteristic effects of histamine by blocking its access to the receptor site in the cell, thus preventing the response of the cell to the amine.[5] Chlorpheniramine maleate has been widely used clinically to control respiratory and dermatologic allergies,[6] and to prevent or minimize reactions to therapeutic allergens,[7] blood transfusions,[8] or penicillin.[9]

MATERIALS AND METHODS

d-chlorpheniramine was introduced recently for clinical trial in respiratory and dermatologic allergies. It is available as 2-mg. tablets or as repeat action tablets* containing 3 mg. in the outer layer for immediate release and 3 mg. in a protected core for release four hours after ingestion. Early clinical trials were conducted to evaluate its effectiveness, duration of action, and side effects.

One hundred patients have been treated to date. Those who had previously received chlorpheniramine maleate were switched to *d*-chlorpheniramine in equipotent doses, and

*Polaramine®, Schering Corporation, Bloomfield, New Jersey.

2. Labelle, A., & Tislow, R., *J. Pharmacol. & Exper. Therap.*, 113:72-88,1955.
3. Roth, F. E., & Govier, W. M., *J. Pharmacol. & Exper. Therap.*, 124:318-349,1958.
4. Cronin, M. T. I., et al., Report to the Schering Corporation, 1958.

*Repetabs®, Schering Corporation, Bloomfield, New Jersey.

5. Goodman, L. S., & Gilman, A., Pharmacological Basis of Therapeutics, Second Edition, Macmillan Co., New York, 1955, pg. 656-662.
6. Packard, L. A., *Eye, Ear, Nose and Throat Month.*, 37:257-260,1958.
7. Silbert, N. E., *Ann. Allergy*, 10:465-468,1952.
8. Offenkrantz, F. M., & Babcock, G., *A.M.A. Arch. Surg.*, 76:379-383,1958.
9. Frankel, D. B., & Stutsman, R. E., *Ann. Allergy*, 13:563-570,1955.

new patients were started on the latter drug. Most patients received a 6 mg. repeat action tablet twice daily. A few adults received the 2 mg. tablet in total doses of 8 or 12 mg. daily, and children received 4 or 6 mg. daily.

RESULTS

Preliminary clinical experience tends to confirm the laboratory studies. The drug takes effect rapidly, usually within 10 to 30 minutes, and it has a significantly long duration of action. The drug is twice as potent as chlorpheniramine maleate. The effect of 12 mg. of the latter was equaled or exceeded by 6 mg. of *d*-chlorpheniramine.

Most responsive allergies were controlled by two 6 mg. repeat action tablets daily. The drug appeared to be especially effective in patients who presented sudden, acute allergy symptoms. In some cases of severe allergy this antihistamine may obviate the need for steroid therapy.

SIDE EFFECTS

The lower dosage made possible by the increased potency of the drug resulted in a marked reduction of typical antihistaminic side effects such as drowsiness, xerostomia, nausea, or dizziness. Only two of 100 patients reported drowsiness. In one case this effect disappeared after a day in spite of continued therapy; in the other it was relieved by slightly reducing the dosage. A third patient noted mild xerostomia, which also was obviated by reducing the dose. One patient thought there had been a stimulating effect.

CONCLUSIONS

1. In 100 patients treated for a wide variety of allergy symptoms the drug was noted to take effect rapidly, usually within 10 to 30 minutes, and to have a significantly long duration of action.

2. The medication proved to be especially effective in patients who presented sudden, acute allergy symptoms.

3. A marked reduction of typical antihistaminic side effects such as drowsiness, xerostomia, nausea or dizziness was noted.◀

Histoplasmosis as a Cause of Solitary Pulmonary Granulomas

Twenty solitary pulmonary granulomas (coin lesions) were surgically excised from patients aged 26 to 65 years. The case histories were reviewed with particular emphasis on the results of skin tests, smears and cultures of sputum, and cultures of the excised nodules.

Histoplasma capsulatum was histologically identified as 35% of the 20. Identification of this organism is facilitated in tissue sections by the use of the Grocott methenamine-silver technique.

It is concluded that H. capsulatum may represent an important cause of solitary pulmonary nodules in persons now residing in Pennsylvania, reputedly a non-endemic area. The individuals studied may have acquired their infection in other areas. Soil and skin tests in this area may be of value in clarifying this matter.

Fisher, E. R., & Rock, J. A., *Pennsylvania M.J.*, 62: 197-200,1959.

ORIGINAL ARTICLE

The Surgical Repair of Diastasis Recti

Massive overlap of abdominal wall flaps has been used successfully in the repair of this clinical entity

EDWARD A. FITCH, M.D., *Philadelphia, Pennsylvania*

A review of the literature as far back as 1915 reveals no article classified under the category of "diastasis recti." This condition differs sufficiently from ventral, incisional and umbilical hernia, and muscular agenesis, to warrant its consideration as a separate entity.

The following scheme of classification is proposed:

DIASTASIS RECTI ABDOMINIS

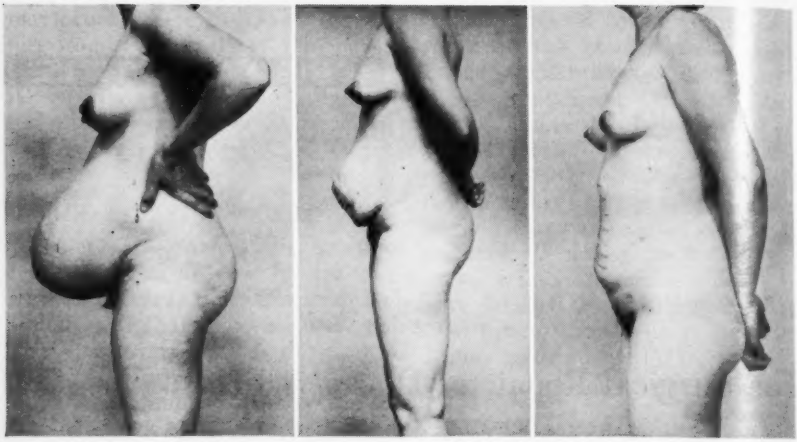
ETIOLOGICAL

Congenital
  Transient
  Permanent
Acquired
  Primary (idiopathic)
  Secondary
    Postpartum
    Post-incisional
    Miscellaneous
      Ascites
      Obesity
      Intra-abdominal
Combined (as part of other musculo-fascial defects, congenital or acquired)

ANATOMICAL

Complete (xiphi-public)
Partial (epigastric, hypogastric, etc.)

The congenital variant is usually mild in degree and frequently self-correcting. Occasionally cases have developed in adults with no discernible cause. The largest number of cases by far are seen in the multiparous patient. Midline incisions may be followed by widening of the fascial scar. Other causes of abdominal distension are rarely followed by widen-



LEFT: Patient with full term pregnancy complicated by severe diastasis recti. CENTER: Patient following delivery by internal podalic version. Most of the intestines reside in the flaccid sac between the separated recti muscles. RIGHT: Patient following repair of diastasis recti.

ing of the linea alba. Diastasis recti is found combined with other musculofascial lesions, both congenital and acquired, including those cases of true hernia occurring through the stretched fascia of a true diastasis recti abdominis.

The usual indication for repair is the desire of the patient to rid herself of a cosmetic defect. When symptoms occur, they are similar to those of any large ventral hernia. Unlike ventral and umbilical herniae, diastasis recti rarely involves serious complications as strangulation, incarceration, or adhesive intestinal obstruction.

PREOPERATIVE PREPARATION

Frequently it is desirable to precede surgery with a period of appropriate exercises to increase the bulk of the recti and add strength to the fascia. Obesity control is desirable. Conception control may be applicable. An interval of at least six weeks should elapse following childbirth to allow the "softening" effect of pregnancy hormones to dissipate.

OPERATIVE TECHNIQUE

Two repair techniques are used.

In the first, a long elipse of skin from xiphoid to symphysis pubis is excised, and the incision carried down to the fascia. The fascia is cleaned laterally to the palpable recti muscles. Both rectus sheaths are opened close to their medial margins and the posterior sheath and remaining parites opened in the midline. The posterior sheaths are then overlapped sufficiently to draw the recti muscles into an overlapping position and united by interrupted cotton or silk sutures. The anterior sheaths are overlapped and sutured in a similar manner.

In the second technique, the entire thickness of the abdominal wall is opened in the midline after excision of the excess skin, a triangular portion of peritoneum and extraperi-

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toneal fat is cleaned off the left lower quadrant area to allow for firmer union of the overlapping flaps. Massive overlap of the abdominal wall flaps places the left denuded flap superficial to the right; interrupted nonabsorbable sutures fix the flaps in place and active suction by perforated catheters in the subcutaneous space assures against serum accumulation.

POSTOPERATIVE CARE

Abdominal distention is prevented by gastric or intestinal suction until bowel sounds and flatus are evident. Coughing, straining, singultus and vomiting are prevented. Ambulation is early with the aid of an abdominal binder for the first 10 days. Ambulation without straining is the keynote for the first three weeks. From the third through the sixth week, slowly increasing activity is allowed. Return to full activity is gradually allowed during the sixth through the eighth week. The use of abdominal supports is allowed but not encouraged. The patient is instructed in the development of subconscious, sustained abdominal musculature tonus.

CLINICAL MATERIAL

Seven cases of diastasis recti abdominis form the basis for this report. Type 1 repair was used in two cases and the remainder were repaired by the Type 2 technique. The follow-up periods have been from eight months to three years. There have been no recurrences. One patient has had two subsequent full term pregnancies. Five cases were of the postpartum type, one postincisional, and one combined type with congenital deficiency of the abdominal musculature.◀

ORIGINAL ARTICLE

Triamcinolone: A Potent Anti-Inflammatory, Sodium Excreting Adrenosteroid

Anti-inflammatory activity is four to six times that of hydrocortisone, with replacement of sodium retention by sodium diuresis

THOMAS HODGE McGAVACK, M.D., *Martinsburg, West Virginia*

The partial synthesis of an adrenocortical hormone, desoxycorticosterone, was first accomplished in 1937.[1] Since that time a variety of compounds containing the cyclopentenophenanthrene nucleus have been added to make up quite a list. The discovery that an adrenocortical steroid could be useful in a disease as widespread and as crippling as rheumatoid arthritis[2] intensified severalfold the interest in seaching for other compounds with greater "anti-inflammatory" and "anti-allergic" activity.

Attention has recently been called to the importance of developing compounds in which these properties are maintained, while sodium retaining activity is decreased or abolished.[3,4] Selected from a large group of compounds, triamcinolone* was shown to possess anti-inflammatory activity four to six times that of hydrocortisone with the replacement of sodium retention by sodium diuresis. The chemical structure of this compound differs from that of prednisolone by the presence of a fluorine atom in the alpha position at carbon atom 9, and

1. Steiger, M., & Reichstein, T., *Nature*, (London), 139:925,1937.
2. Hench, P. S., et al., *Proc. Staff Meet. Mayo Clin.*, 24:181,1949.

*Aristocort,® Lederle Laboratories, Pearl River, New York.

3. Bernstein, S., *Rec. Prog. Horm. Res.*, 14:1,1958.
4. Drill, V. A., & Riegel, B., *Rec. Prog. Horm. Res.*, 14:29,1958.

a hydroxyl group in the alpha position at carbon atom 16. Through the changes at carbon atom 9 all activities of the parent prednisolone molecule are intensified. The addition of the hydroxyl group in the position noted results in the abolition of the sodium retaining activity while maintaining 1.5 to 2 times the anti-inflammatory activity of prednisolone.

Lacking the strong tendency of most such available compounds to retain water and sodium, triamcinolone should be useful in cardiac failure with edema, in other forms of edema, in the elderly and the obese with poor cardiac reserve, and in any condition such as hypertension, in which the retention of salt and water is highly undesirable.

CLINICAL APPLICATIONS OF TRIAMCINOLONE

Spontaneous remissions may occur in a majority of the conditions for which the "anti-inflammatory" steroids are used. The large doses necessary for the control of such conditions are apt to cause side effects. Nevertheless, from the reports of treatment with triamcinolone,[5-21] and our own experiences,[22] it seems possible to gain a fairly clear idea of its spheres of usefulness and to make a comparison with the older and more recently developed steroids.

Among many diseases which respond to "anti-inflammatory" steroids there are no sharply defined boundaries; e.g., in rheumatoid arthritis a vasculitis is commonly present and may play a causative, rather than a secondary, role in the development of some of the joint phenomena.[23] Under such conditions, arthritis might be looked upon as primarily a vascular disease. Diseases such as lupus erythematosus could be considered allergic or hypergic in nature.

ARTHRITIS

Triamcinolone has been used in rheumatoid arthritis,[9,11-13,16,17,21] osteoarthritis,[11,12,17] "nonarticular rheumatism",[9] palindromic rheumatism[9] and psoriatic arthritis.[15,19,22] In rheumatoid arthritis good control has been achieved in from 60[13] to 100[21] per cent of the patients studied. A major factor limiting its usefulness has been the appearance of Cushing-like phenomena on long continued use. In arthritis, initial doses have ranged from 6 to 25 mg. daily with a mode of from 12 to 16 mg. daily, and maintenance doses from 4 to 12 mg. daily. If the amount used daily is less than 4 mg. it may be given as a single dose in the morning.[24]

OSTEOARTHRITIS

Here a single daily dose is usually sufficient.[17] When major manifestations are localized, injections of 10 to 25 mg. of the diacetate into the joint have proved satisfactory. Such injec-

5. Curd, G. W., & Spurr, C. L., *Am. J. Med.*, 25: 116,1958.
6. Dameshek, W., et al., *J.A.M.A.*, 166:1805,1958.
7. Dubois, E. L., *Metabolism*, 7:509,1958.
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tions can be repeated at necessary intervals with little or no fear of systemic or side effects.

In using triamcinolone or any other adrenal steroid in the treatment of rheumatoid or osteoarthritis, the objectives of therapy must be seriously considered. Hartung[11,12] feels that such therapy should be reserved for four distinct situations:

1. When the rheumatoid arthritis is fulminating and does not promptly respond to adequate salicylate therapy.

2. When we are unable to maintain the chronic case in reasonable comfort after a thorough trial of rest, corrective exercises, salicylates and constitutional therapy.

3. When gold salt therapy fails after an adequate trial and the conditions mentioned in No. 2 above prevail.

4. As a temporary measure just before, during, and after some orthopedic and rehabilitation procedures.

In view of the rather complete relief which adrenosteroid therapy can afford in arthritis,[17] these restrictions seem hardly justified. Some studies[23] may indicate that aspirin is almost as good as steroid therapy. However, the author doubts that any practicing physician can claim results in this crippling disease prior to the advent of steroids that in any way match those obtained since these agents have been available.

SIDE EFFECTS

A limiting factor to the usage of adrenosteroids in arthritis is the incidence of side effects, some of which may have serious consequences. The appearance of the more severe of these, such as diabetes, peptic ulcer and osteoporosis, will justify the discontinuance of the steroid, a trial of a second steroid, or at least a reduction in dosage. There is considerable opposition to the use of "counteracting" therapy, such as insulin for patients showing decrease in sugar tolerance, alkalis for those with gastro-intestinal symptoms, and estrogens and androgens for those with manifestations of osteoporosis. If one or two joints are more involved than others, side effects may often be avoided by using small oral doses, 2 to 4 mg. daily, combined with local injection of the involved joints.

UNUSUAL FORMS OF ARTHRITIS

Other forms of arthritis, including psoriatic, monarticular and palindromic, can be handled by very much the same regime with equally favorable results.[9,15,17,19] In the treatment of arthritis, triamcinolone, weight for weight, has been found to be as effective as, or, one and one-half times as effective as prednisolone.[11,12,17,18]

ALLERGIES

Both hay fever and bronchial asthma have been treated with triamcinolone with good results.[10,17,20] Patients transferred from prednisolone required two-thirds the dose of the former compound. Maintenance dosages have varied from 2 to 20 mg., with an average of approximately 8 mg. daily. On such dosages some observers have noted few if any side effects, while others have found that 20 per cent of the cases were returned to previous medication because of untoward responses.[10,17,20]

SKIN ALLERGIES

In this realm triamcinolone has been employed chiefly for the treatment of the atopic and exfoliative forms of dermatitis.[10,17-19] Eighty to 100 per

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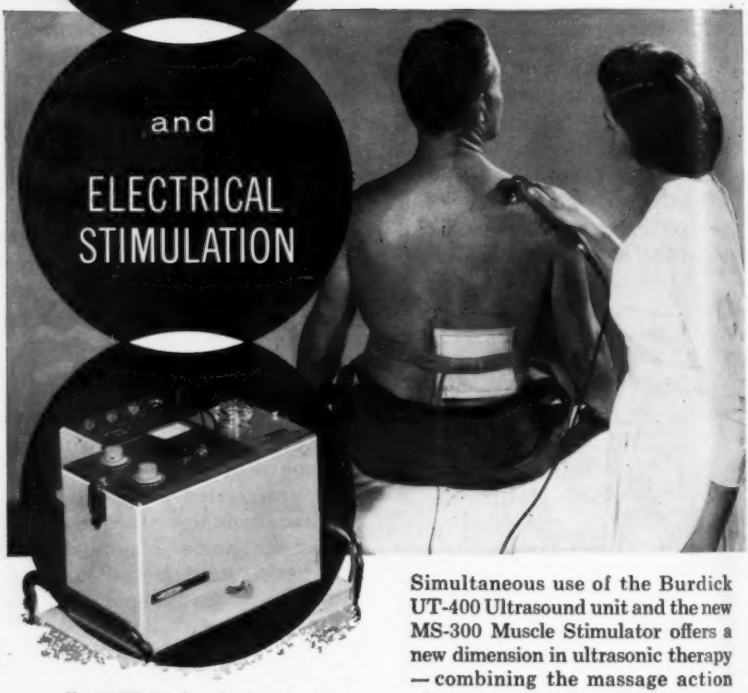

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cent of patients have obtained major or complete relief from such therapy.[10,18] However, "mooning" of the face has been reported in some 50 per cent in one series of cases.[18] Slightly less than one-fourth of the subjects in a second series have been transferred to other therapy because of side effects.[10] Maintenance dosages in these conditions have ranged from 2 to 24 mg. daily with the mode between 8 and 12 mg. daily. Some tendency to recurrence of the skin condition has occurred whenever steroid therapy was stopped. It is our belief that any cortisone-like steroid should be used as an adjuvant type of therapy.

If possible, the doses of a steroid in dermatologic conditions should be below those commonly associated with ACTH suppression, as long-term therapy is usually necessary to achieve any permanent result. In these conditions, triamcinolone has been found to be one and one half to two times as active as prednisolone, weight for weight.

PSORIASIS PRONE TO REMISSIONS

Nearly all patients with psoriasis respond favorably to a change in physicians and medications. However, several reports have appeared of responses to the use of triamcinolone, more dramatic than those seen by the same observers to any of the other 11-oxysteroids tried.[15,17,19] Of 60 patients, 60 per cent were free of lesions within several weeks of beginning therapy and have remained so throughout 12 months of observation.[19] Eight of 14 patients were completely relieved of all skin lesions, whereas, two of the 14 could be considered complete failures.[15]

On the basis of history and physical findings it was not possible to determine which patients with psoriasis would and which would not respond. It was found, however, that the refractory patients were hyporeactive to the local effects of triamcinolone.[19] A one per cent suspension of triamcinolone produced "a sharp circumscribed area of complete involution" at the site of application in those subjects who responded to the systemic use of the drug, whereas no response was observed in those refractory to the systemic action of triamcinolone. In the author's hands, none of the older steroids has caused complete involution of all of the lesions of psoriasis, unless dosages were large enough to produce a high incidence of side effects. Triamcinolone in moderate, well tolerated doses has maintained good control. Patients have now gone for more than a year on small maintenance dosages without the return of lesions. For the control of psoriasis, initial doses have varied from 8 to 32 mg., maintenance doses from 2 to 12 mg.

BLOOD DYSCRASIAS

Leukemia[5] and idiopathic thrombocytopenic purpura[6] have both responded promptly to the administration of triamcinolone. Initial dosages need to be large, sometimes as high as 80 mg. daily. Once complete control of symptoms is achieved, this can be reduced by at least 50 per cent. Thus far such massive dosages have not caused edema. In all cases previously maintained on prednisolone, formerly present edema disappeared while treatment was continued.

COLLAGEN DISEASES

Of all these, lupus erythematosus has been the one most adequately studied during treatment with triamcinolone.[5,7-9,17,21] Several patients

were followed for 13 months, and 29 for an average of four and a half months while they were taking the drug. Dosages to control varied from 4 to 40 mg. daily, with an average of 21 mg., while maintenance doses ranged from 8 to 96 mg., average 26 mg. The symptoms of 27 of these 29 patients were completely controlled. The two failures were patients with severe renal involvement. The initial doses of drug were low, because a majority of these patients were switched from prednisolone to triamcinolone. In the management of lupus erythematosus it was shown that triamcinolone is one and one third times as active as prednisolone.[7,8] While side effects were produced in 45 per cent of the patients treated for lupus erythematosus, they were usually not severe. Moreover, edema, frequently seen when the older stroids were used, disappeared under treatment with triamcinolone.

Patients with periarteritis nodosa have been controlled as well with triamcinolone as with the older steroids, sometimes better.[17] Initial doses have been 12 to 16 mg. daily, maintenance doses 4 to 12 mg.

The progress of widely and rapidly metastasizing lymphosarcoma appears to have been arrested in one case by the use of triamcinolone[21] in daily doses of 12 to 16 mg.

MISCELLANEOUS CONDITIONS

Four children, age one and one-half to four years, with "'typical findings" of nephrosis, obtained prompt and prolonged remissions without undesirable side effects while taking 4 to 20 mg. of triamcinolone daily; a patient with an elevated blood urea nitrogen did not respond. In those who responded, steroid therapy was discontinued after all laboratory findings had returned to normal. At the time of the report, the patients had been off the drug for periods of two to eight months, and in no instance had developed any clinical or chemical evidences of recurrence.

The anemia of sprue has reverted to normal promptly following the use of triamcinolone.[21]

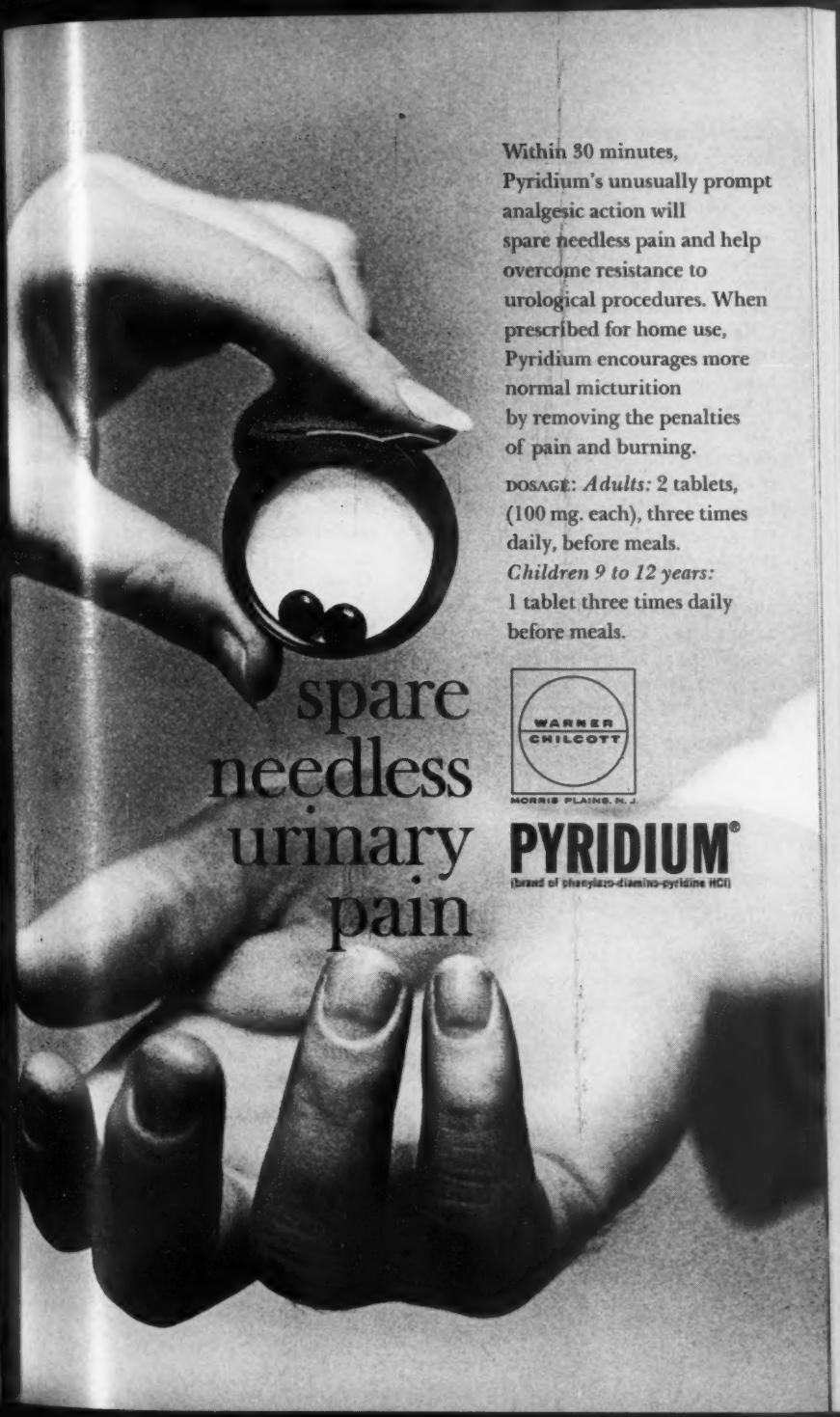
Triamcinolone can be given without fear in patients with edema, and instances of refractory cardiac edema have improved through its usage.[17] Dosages varying from 4 to 12 mg. daily are useful adjuncts in cardiac therapy.

In advanced cases of chronic pulmonary emphysema, triamcinolone has been added to other therapy in dosages of 8 to 12 mg. daily, with some evidences of immediate relief and even more sustained improvement on continuing the drug for periods up to four months.[17,22] Timed vital capacity, maximum breathing capacity, residual pulmonary volume, the carbon dioxide of alveolar and expired air, and blood oxygen saturation have tended to return toward normal during such therapy. It is as yet too early to determine whether or not any of these favorable changes can become permanent.

In advanced cirrhosis of the liver triamcinolone has not helped and may have aggravated the status of four such patients to whom it was given.[17,22]

DOSAGE

Unless faced with an emergency such as severe lupus, acute leukemia, idiopathic thrombocytopenic purpura with severe hemorrhage, periarteritis nodosa, etc., the tendency is to start with more modest doses and gradually increase until control is established. With triamcinolone, this method is



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very effective and usually prevents the appearance of side effects or defers their appearance for months. In acute emergencies, doses up to 80 mg. daily have been used,[5] but it is rarely necessary to exceed 20 mg., even in the most severe conditions. For the more chronic conditions in which an anti-inflammatory steroid is applicable, initial daily doses of from 12 to 16 mg. have been sufficient and maintenance doses have varied from 2 to 12 mg. After all manifestations have been controlled for one week, the reduction of dosage should be initiated and continued at suitable intervals until the minimal effective amount is reached. Should any symptoms of the disease state reappear the patient is immediately returned to the last dosage on which he was symptom-free. He should be maintained at that level for at least a month before further reduction is attempted.

SIDE EFFECTS

Several investigators[5,6,14,21] have seen no undesirable manifestations; others reported them in 100 per cent of their cases.[11-13] It is doubtful that any one of the 11-oxysteroids thus far used for its anti-inflammatory or anti-allergic activity is free of side effects. An accurate evaluation of the incidence of such effects cannot be made on periods of treatment under four months.

In some degree all of this group of steroids share the same side effects with one notable exception: Edema and hypertension have not as yet been described in conjunction with the administration of either triamcinolone or dexamethasone. Indeed, these manifestations have disappeared when previously present or produced by any of the other corticoids mentioned[12,17,22] above.

MOONING, ACNE, HIRSUTISM, STRIAE AND ECCHYMOSES

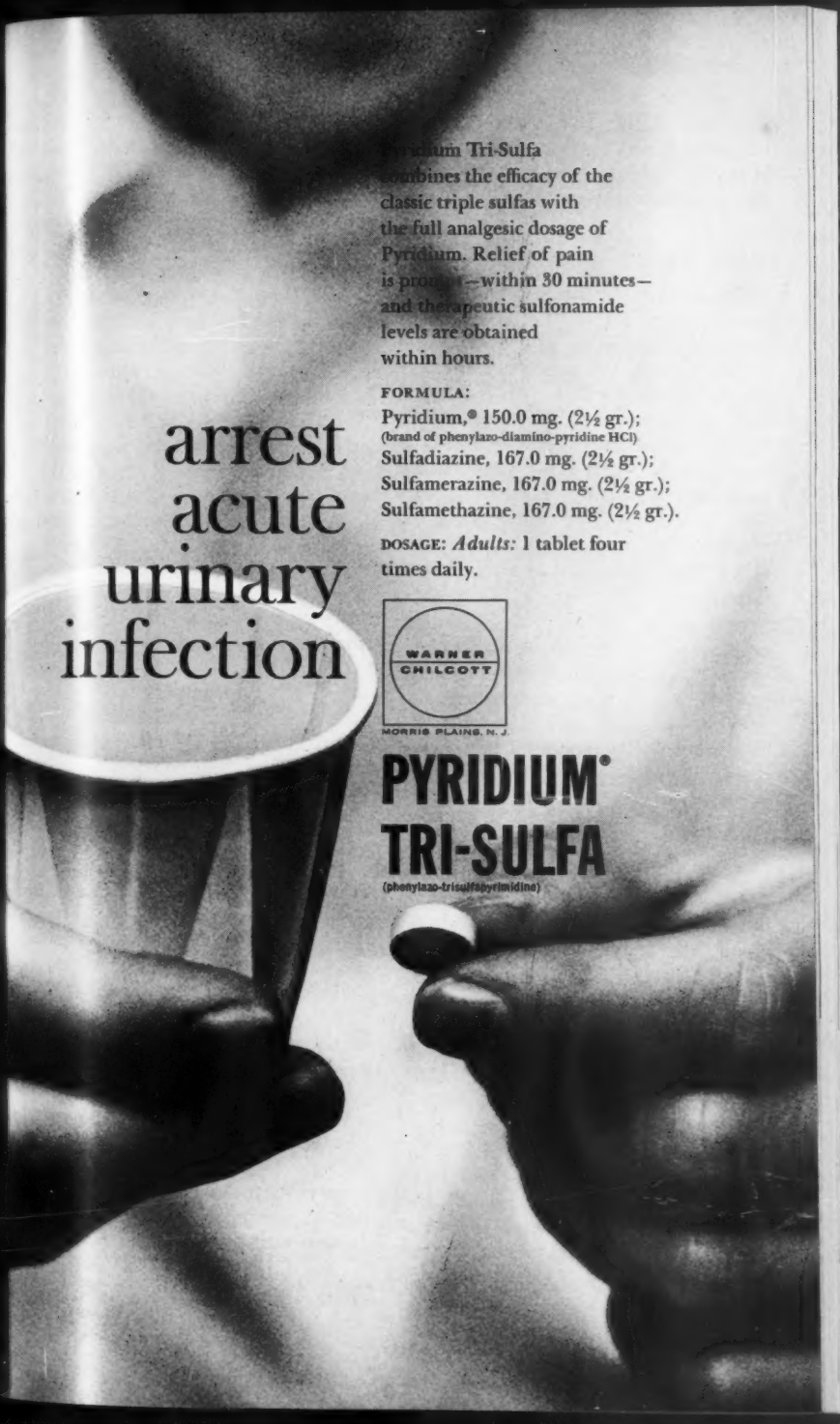
These effects have been more commonly produced by cortisone, cortisol and their delta-1 congeners. However, one observer using triamcinolone in 26 dermatologic patients for periods of one to three and one-half months observed mooning in 50 per cent; it was present in 10 per cent of the present series.[22] Some have found this to be a troublesome feature only in women.[11,12] One of 65 men had acne as a result of treatment with triamcinolone. When previously produced by cortisol or prednisolone, this manifestation has been seen to disappear while therapeutically equivalent doses of triamcinolone were employed. Hirsutism, striae, and ecchymoses have all been described with triamcinolone, but only the last appears to occur with this drug as frequently as with its progenitors.

DIGESTIVE CONDITIONS

Epigastric distress and peptic ulcer are least often found with triamcinolone.[13] Peptic ulcer was observed in one of 14 patients treated with triamcinolone, and in 27 of 61 receiving prednisone in equivalent therapeutic amounts.[16] It was noted that the ulcers produced by steroid therapy do not resemble peptic ulcer in character or location. The healing of previously present peptic ulcers has been observed while the patient remained on steroid therapy.

METABOLIC CONDITIONS

A lowering of sugar tolerance has been ascribed to triamcinolone but this has been seen less frequently than with other steroids. Under certain conditions, losses of calcium, phosphorus and nitrogen have been observed during the administration of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any one of the 11-oxysteroids, and triamicinolone is no exception. These losses are greatest with dexamethasone and possibly least with triamcinolone.[5,25,26]

MISCELLANEOUS

Generalized headaches have been produced by all of the 11-oxycorticoids. The inhibition of growth in association with 11-oxysteroid therapy has been observed to vary directly with the degree of ACTH suppression. Triamcinolone is as powerful as its congeners in this regard. Generalized weakness and easy fatigability are seen in a few of the subjects on triamcinolone therapy. This has been observed with moderate as well as with large doses.[7,8]

It is as yet too early to determine whether or not the newer compounds, triamcinolone, methylprednisolone, and dexamethasone, will cause osteoporosis and, if so, to what degree. All of the earlier compounds have been shown capable of producing osteoporosis. In view of the marked influence of dexamethasone on calcium excretion,[25] there would seem to be little doubt that it will deplete the bone of calcium. Whether triamcinolone and methyl-prednisolone will share this activity is not yet established.

Psychic unrest and unwarranted euphoria, usual sequelae of earlier steroidal therapy, were most uncommonly observed when triamcinolone was used.[11,12,17,22] Muscular weakness and fatigue of severe degree have been found in conjunction with the administration of triamcinolone.[7,26] Pechet et al. have connected this with marked losses of potassium,[26] but neither the latter[9,13,14,17] nor an association of the weakness with alterations in potassium metabolism[7-9,12,17,27,28] has been seen by others. One observer connects these symptoms with the commonly seen anorexia and weight loss.[9] In doses larger than those needed for other than the most severe emergencies (42 to 82 mg.) negative balances for potassium, sodium and chloride have been observed.[5] Loss of weight during the early days of treatment with triamcinolone is common, probably due chiefly, if not entirely, to the loss of water and salt. Weight is stabilized at a new and usually lower level as treatment is continued.[9,17,22]

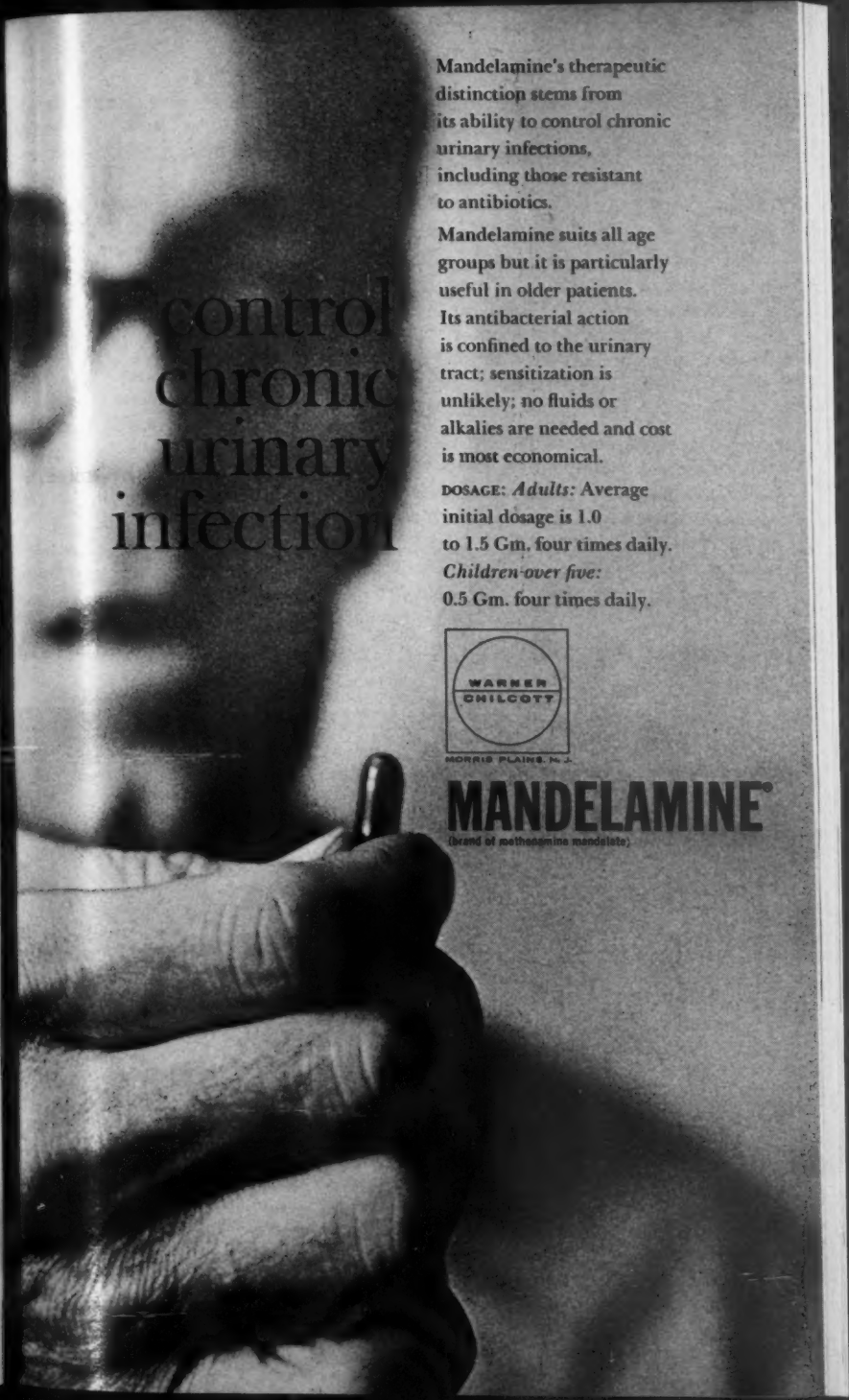
CONCLUSIONS

Comparisons of the activities of adrenosteroids of the 11-oxycorticoid type are difficult to make because of the widely variable approaches of different observers; variations in dosage and duration of treatment from investigator to investigator, and among the patients of a single worker; and lack of uniform criteria for collecting, evaluating and recording data.

Despite these difficulties it would appear that the newer synthetic corticoids—methylprednisolone, triamcinolone and dexamethasone—possess some virtues as anti-inflammatory and anti-allergic agents not shared by their earlier developed congeners cortisone, cortisol, prednisone and prednisolone.

All tend to promote the excretion of salt and water in this descending order: triamcinolone, dexamethasone, and methylprednisolone. These properties further promptness of action in the inflammatory and allergic diseases for which these drugs are

25. Bunim, J. J., et al., *Arthritis and Rheumatism*, 1:513,1958.
26. Pechet, M. M., et al., *J. Clin. Invest.*, 37:921, 1958.
27. Wozniak, L. A., et al., *Fed. Proc.*, 17:421,1958.
28. Kupperman, H. S., et al., *Metabolism*, 7:403, 1958.



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normally indicated, enabling the physician to employ them with safety in the older person who has potential or actual cardiac failure. In this regard, triamcinolone would appear to be the best of the three drugs.

2. Psychic aberrations are minimized, having been reported most frequently with methylprednisolone, seldom, if at all, with the other two drugs. They appear fairly frequently with the older compounds.

3. Hypertension has not accompanied or been caused by any one of the three newer compounds, and when due to a previously used steroid, has usually disappeared when triamcinolone, methylprednisolone or dexamethasone has been employed.

4. An increase in appetite has frequently followed the administration of methylprednisolone, but rarely that of triamcinolone or dexamethasone. Indeed, loss of weight has been the rule, although this has not been excessive.

5. All three of the newer steroids share the ability of the older compounds to excrete calcium. This is usually negligible in amount with methylprednisolone and triamcinolone, but is so marked with dexamethasone as to represent a contraindication to its prolonged use.

6. Administration of any one of the three newer compounds is prone to cause decrease in sugar tolerance less marked in incidence and severity than that observed with any of their older analogues.

7. The descending order of anti-inflammatory and anti-allergic potency of the newer compounds, weight for weight, is dexamethasone, triamcinolone, and methylprednisolone.◀

ORIGINAL ARTICLE

Treatment of Renal Failure

Renal failure presents unique problems in diagnosis, treatment and regulation of kidney function

KEEHN W. BERRY, JR., M.D., *Birmingham, Alabama*

The physician's first obligation on seeing a patient with azotemia is to determine its cause: This may be unilateral renal disease, post-renal obstruction, acute renal failure due to acute renal anoxia with tubular degeneration (lower-nephron nephrosis), all of which are potentially curable. Azotemia, or uremia, is more commonly due to the end stage of chronic glomerulonephritis, a chronic hyelonephritis, and under these circumstances therapy is directed at prolonging life and comfort.

CLASSIFICATION

Renal failure may be either acute or chronic. Acute renal failure may occur in the course of chronic renal disease, or may be secondary to disease not primarily of the kidneys, *e.g.*, renal shutdown occurring postoperatively (particularly in patients who have been in shock), transfusion reaction, and reaction following exogenous poisons. Recognized early and treated adequately, the cure rate is very high. On the other hand, therapy in chronic renal failure as seen in glomerulonephritis, pyelonephritis or polycystic kidney requires an approach directed at maintenance of the internal environment and some regulation of renal function in an effort to prolong life.

TREATMENT OF ACUTE RENAL FAILURE

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24 hours. Therapy should be directed at avoiding over-hydration, rapid accumulation of nitrogenous waste products as manifested by elevation of the blood urea nitrogen or nonprotein nitrogen, and maintaining electrolyte balance and nutrition.

1. Avoidance of over-hydration. In the oliguric patient, in the absence of marked fever with sweating or marked hyperventilation which would increase insensible fluid loss, 0.5 to 0.6 cc. of water per kg. of body weight per hour is used as a baseline for calculating insensible loss. Any other fluid loss by gastric tube, vomiting, or diarrhea, must also be taken into consideration. The oliguric patient of 70 kg. weight should have fluid replacement of 400 cc. per day plus a volume equal to the output of urine and gastrointestinal tract. The weight of the patient may be used to determine whether or not fluid retention is occurring. Maintenance of weight or gain in weight must be assumed to be the result of fluid retention. In the patient who can take fluids by mouth, oral administration of hypertonic glucose or lactose is probably the best method of getting fluid and food into the patient. In the anorectic patient, intravenous infusion of 20 to 50 per cent glucose in water may be accomplished through a plastic catheter which has been threaded into a large vein.

2. Nitrogen retention occurs in these patients, even on a completely protein-free diet, due to endogenous protein catabolism. In the patient with increased metabolism such as that due to fever, endogenous protein breakdown will be increased. Increase in nitrogen production will also occur following trauma. It is impossible to avoid these endogenous sources of nitrogen, but all exogenous nitrogen sources can be cut off by keeping the protein intake at zero. Testosterone propionate may be administered to these patients for the protein-sparing effect. The dose should be 50 mg. intramuscularly the first day and 25 mg. every day or every other day for a week to 10 days.

3. Electrolyte problems in acute renal failure are related particularly to avoidance of hyperpotassemia and regulation of sodium balance. The patient in acute renal failure should receive no potassium unless the level is lowered dangerously by excessive vomiting or diarrhea. Sodium balance requires careful observation and evaluation of the individual patient. Generally a low serum sodium in this situation is the result of a dilutional hyponatremia, most commonly the result of overzealous administration of hypotonic fluids. The only indication for administering sodium to a patient with acute renal failure is excessive loss of sodium-containing fluid through the gastrointestinal tract.

Other electrolytes that should be mentioned are calcium and phosphorus. It is frequently necessary to administer aluminum hydroxide gel to bind phosphorus so that adequate calcium absorption can take place, and so that phosphorus absorption does not occur.

4. Maintenance of nutrition has been covered under discussion of fluid balance.

Other problems that arise are related to sedation, and here some of the phenothiazine derivatives may be used both as sedatives and as help in preventing nausea. Congestive failure should be treated by digitalis, with the realization that it will probably not be as effective as in treatment of the more common forms of congestive

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in chronic onstipation

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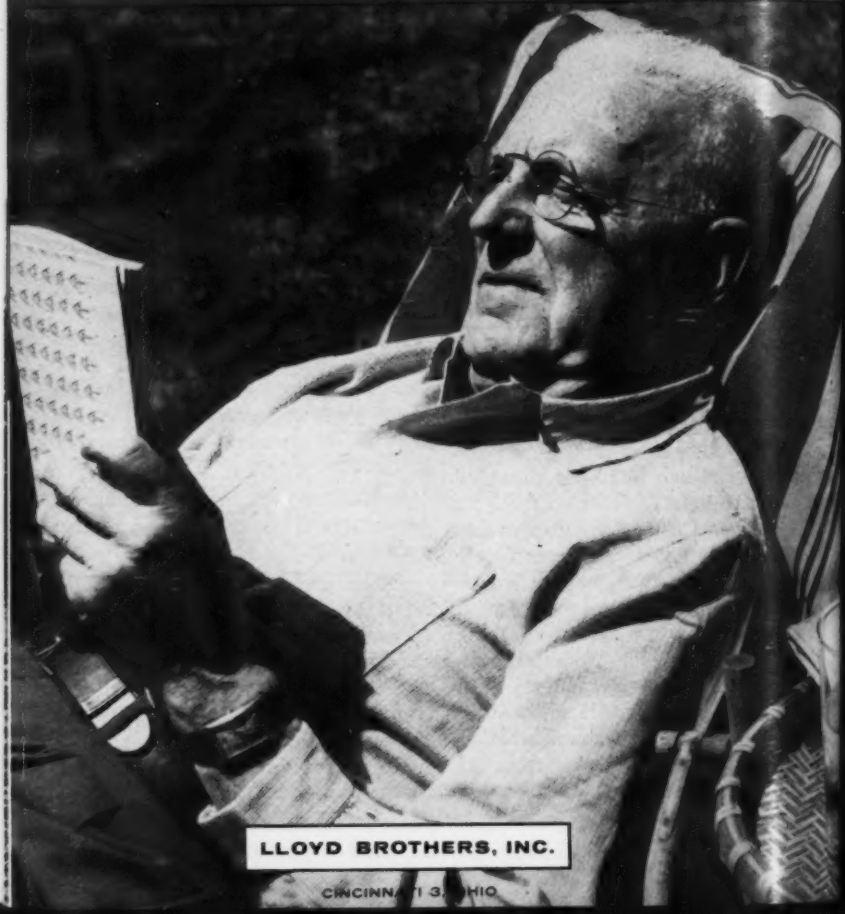

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failure. The hypopotassemic patient is extremely sensitive to the toxic effects of digitalis. As to use of the artificial kidney, the reader is referred to the special literature.

THE DIURETIC PHASE OF ACUTE RENAL FAILURE

This phase accounts for up to one-quarter of the deaths following acute renal failure, and may occur at any time from the second or third day through the twentieth. This phase demands careful observation of sodium and potassium intake and output. Many of these patients are clinically over-hydrated at the onset of diuresis, and to force fluids on them will be harmful. Some patients retain sodium during the diuretic phase. Serum potassium will continue to rise for a few days after diuresis has started, but as soon as the urine volume exceeds 1500 cc. per day, dietary potassium restriction should cease, and administration of large amounts orally or parenterally may occasionally be necessary to replace that lost in the urine. It may be six months or more before normal kidney function returns, particularly the concentrating power. Some patients never return to a completely normal state.

These principles of treatment apply also to acute renal failure occurring in the course of chronic renal disease.

POTASSIUM INTOXICATION

This state deserves special attention. In acute renal shutdown following war wounds it was noted that death from potassium intoxication occurred within five days unless the artificial kidney was used. For lowering the elevated serum potassium there are other simpler measures. It is important to avoid potassium intake. Vomiting and diarrhea occur with uremia and may help prevent potassium excess. Gastric suction may be of some value in removing potassium. Small intestinal lavage has been advocated. The carboxylic exchange resins have been useful. The hydrogen exchange resin is probably preferable to that containing sodium or potassium. It may be given orally in a 15 to 20 per cent solution containing 45 to 50 gm. per day of the resin, or may be given by enema, 50 gm. of resin in water to make 150 to 200 cc. of solution.

Infusion of calcium solution will reverse acute electrocardiographic signs of hyperpotassemia, as will glucose and insulin infusions, or infusion of 3 to 5 per cent saline solutions in doses of 100 to 200 cc.

CHRONIC RENAL FAILURE

The treatment of chronic renal failure involves essentially the same principles as outlined above, but with certain significant differences. The force-fluids attitude which has been advocated in past years should be discarded. It has been demonstrated that people with chronic renal failure are capable of some variation in solute and fluid excretion. Adaptation to water or salt loading or depletion is slow, however, and high water intake can easily induce water intoxication. Not enough increase in solute excretion is effected to warrant the danger involved in forcing fluids. These patients should be encouraged to take adequate liquids, but it is not necessary to force extra fluids. Excessive fluid loss, as by vomiting or diarrhea, must quickly be replaced because excessive dehydration can precipitate irreversible renal failure. It might prove dangerous to dehydrate patients in preparation for concentrating tests or other studies of

renal function. Renal failure has occurred as the result of dehydration from castor oil in preparation for an I.V. pyelogram.

Nitrogen retention may indeed be a problem in a patient with chronic renal failure, but it must also be realized that urea is an excellent osmotic diuretic, and many patients can go for years with significant elevation of the blood urea nitrogen and remain mentally alert and clear. With marked nitrogen retention or during stress states where acute renal failure may occur, protein restriction is indicated, but for the most part the diet may be normal in protein intake.

ELECTROLYTE DISTURBANCES

Electrolyte disturbances are extremely common in this group of patients, and are often due to injudicious restrictions of sodium and potassium. Inability to conserve sodium is a characteristic of early renal failure, and particularly in chronic pyelonephritis a salt-losing syndrome may occur. In the absence of edema or congestive failure, sodium restriction in the chronically azotemic patient is unwise, and may precipitate acute renal failure. Once again, body weight is an excellent means of determining whether fluid, hence sodium, retention is occurring. It should be remembered that sodium chloride contains sodium and chloride in a 1:1 ratio, while the extra-cellular fluid ratio is 1.4:1. It is therefore frequently necessary to administer sodium bicarbonate or sodium lactate either orally or parenterally to these persons over a long period of time to maintain normal levels.

One is often faced with moderate to severe hypertension in the patient with chronic renal disease, and sooner or later a point will be reached where the hypertension or the nitrogen retention or both will no longer be amenable to therapy. In such instances complete sodium restriction should never be practiced, and drastic lowering of the blood pressure as with blocking agents may precipitate irreversible renal failure. When hypertension is secondary to primary renal disease, complete sodium restriction is probably unwise.

As they lose sodium ion, so many patients with chronic renal failure lose potassium ion. While potassium intoxication is the rule in acute renal failure, in chronic renal failure it is more often necessary to administer supplementary potassium salt. In these instances occasional serum potassium levels are of value, and may be necessary when symptoms which may be the result of potassium excess or depletion (unfortunately similar) are observed in the patient.

Calcium and phosphorus metabolism are important in chronic renal disease because of secondary hyperparathyroidism that occurs. Phosphorus retention is obvious. Hypocalcemia is generally thought to be due chiefly to inadequate absorption. This may be in part corrected by the administration of 1 to 3 gm. of calcium lactate by mouth. This may be mixed with an aluminum hydroxide gel and administered three to four times a day. Hypercalcemia is almost never seen in chronic renal failure as the result of secondary hyperparathyroidism. If hypercalcemia occurs, other causes such as primary hyperparathyroidism or excessive intake of milk with absorbable alkali must be considered.

Maintenance of nutrition in these people is often difficult because of the anorexia and nausea that frequently

...umal Robins U.S. Pat. No. 2770649 TABLETS

...of six published clinical studies:

...IN BENEFICIAL IN 92.4% OF ...TAL MUSCLE SPASM CASES

	NO. PATIENTS	RESPONSE			
		"marked"	moderate	slight	none
	33	26	6	1	—
	58	"pronounced" 37	20	—	1
	38	"good" 25	6	—	7
	17	"excellent" 14	2	1	0
	30	"significant" 27	—	2	1
	60	"gratifying" 55	—	—	5
	236	184	34	4	14

- **Highly potent—and long acting.**[1,2,3]
- **Relatively free of adverse side effects.**[1,2,3,5,6]
- **In ordinary dosage, does not reduce muscle strength or reflex activity.**[1]

REFERENCES: 1. Carpenter, E. B.: Southern M. J. 51:627, 1958. 2. Forsyth, H. F.: J.A.M.A. 167:163, 1958. 3. Lewis, W. B.: California Med. 90:26, 1959. 4. O'Doherty, D. S., and Shields, C. D.: J.A.M.A. 167:160, 1958. 5. Park, H. W.: J.A.M.A. 167:168, 1958. 6. Plumb, C. S.: Journal-Lancet 78:531, 1958.

A. H. ROBINS CO., INC., Richmond 20, Virginia

accompany chronic azotemia. Here also the phenothiazine derivatives have proven of value, and frequent small feedings will often be tolerated when single large meals are not. In both acute renal shutdown and chronic renal failure infection is a common cause of death. Any infection should be immediately called to the physician's attention and treated vigorously. Any unexplained decline in the patient with chronic renal disease should always lead the physician to suspect infection.

One word about anemia of chronic failure, and which also may be associated with acute renal failure is in order. Generally speaking, unless the anemia is so marked as to be symptomatic, blood transfusions are contraindicated. They are only of temporary value and a transfusion reaction in a patient with renal disease may prove fatal. This anemia does not respond to any of the usual measures and is frequently tolerated fairly well.◀

Cause of Peptic Ulcer

In the first 500 patients with duodenal ulcer treated by vagotomy and gastroenterostomy in whom the follow-up period has been five years or more, 90% had a good to excellent result. They were relieved of ulcer symptoms and objective evidence of ulcer, and were able to eat a normal diet without medication. Only 0.4% died from the operation, and failure to obtain a good clinical result was usually due to incomplete vagotomy, an inadequate drainage procedure, or both.

Normally a constant secretion of gastric juice occurs in the empty human stomach even though the patient is shielded from the sight, odor, and taste of food. The amount of acid in this secretion is 10 to 20 mEq. in a 12-hour period at night and is largely nervous in origin, since it is almost completely abolished by division of the vagus nerves to the stomach.

Pure gastric juice, as secreted by the fundus of the stomach, has the ability to digest living tissue including the mucosa of the stomach and duodenum, and to produce a defect which closely resembles progressive peptic ulcer as encountered in clinical practice. A gastric content resembling pure gastric juice is present in patients who secrete such large volumes of gastric juice that the neutralizing effect of food and alkaline secretions is overcome.

Peptic ulcers are usually caused by a hypersecretion of gastric juice rather than a local decrease in the resistance of the mucosa. This hypersecretion in patients with duodenal ulcer is of vagus origin, whereas in those with gastric ulcer it is usually of humoral or hormonal origin. Evidence from both the laboratory and the clinic supports these concepts. Gastrojejunal ulcers develop after low gastric resection for duodenal ulcers because the cause of the hypersecretion is nervous, and so is not corrected by excision of the gastric antrum. The relative absence of gastrojejunal ulcers after low gastric resection for gastric ulcer is attributed to the fact that removal of the antrum abolishes the cause of the hypersecretion of gastric juice in these patients.

Dragstedt, L. R., *J.A.M.A.*, 169:83-89,1959.

ORIGINAL ARTICLE

Buclizine Hydrochloride in Obstetrics and Gynecology: A Preliminary Report

Anxiety and tension states in the obstetric or gynecologic patient may be subdued with buclizine hydrochloride

KARL JOHN KARNAKY, M.D.,* *Houston, Texas*

In the field of obstetrics and gynecology, many patients present themselves with complaints which can conceivably be helped by the utilization of appropriate tranquilizing medication. Many patients who come to the office with obstetrical or gynecological complaints also complain of nervousness, restlessness, frequent crying for no reason, and premenstrual symptoms of a disagreeable nature. The wide use of "tranquilizing" medications has included their use in patients in "anxiety tension states." The majority of these patients are active women who carry out their routine activities and require only the supportive effect of this medication. For several years attempts have been made to synthesize preparations that will effectively combat the anxiety state without causing mental lassitude or depression.

It is important to describe in detail exactly what is meant by anxiety complaints. These are patients often seen in obstetrics and gynecology with problems relating to their home life—financial difficulties, sexual difficulties, excessive drinking, suspicion that the husband is running around with other women, the husband plays

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poker one or two nights a week, the boss is coming over for the evening, they have to go out for the evening, and even tension because they are not going out for the evening. Some complain that the children are getting on their nerves because they are playing and fighting in the house whereas previously this wouldn't bother them at all. They may be nervous because of visits from in-laws, or because the baby has a cold, or may have polio, or that cancer may be developing, or because a daughter is now dating and doesn't come home on time, or that the children going out for the evening will have an automobile wreck, or will drink, or will go wrong. These are the common, everyday worries that many women these days are confronted with and when associated with some basic gynecological problem may become greatly magnified.

Of the multitude of tranquilizers available, a number serve their best purpose in psychiatric and severe emotional states. Among a group of far more utilizable compounds for the average person are those of the piperazine group. This report describes clinical experiences over the past year with one such compound, 1-p-chlorobenzhydryl-4-p-tertiarybutylbenzylpiperazine dihydrochloride. Clinically this compound is known as buclizine hydrochloride.*

A group of 68 women patients who have had a variety of complaints in addition to those which might be considered anxiety complaints serve as the basis of this report.

Some of these patients had been on other tranquilizers. In a number of such instances, the therapeutic effects were masked by side reactions prominent enough to warrant discontinuing use of the preparation. Lightheadedness was fairly common among patients who had taken the more potent tranquilizers. These, even in reduced doses, caused side effects such as marked drowsiness, a feeling of being detached, or similar complaints.

Use of buclizine hydrochloride was prompted by the fact that this preparation had been fairly widely used as an antihistamine with evidence of low toxicity and few side reactions.[1] Studies in this country on the antiemetic effect of buclizine-containing compounds suggested a high degree of therapeutic activity.

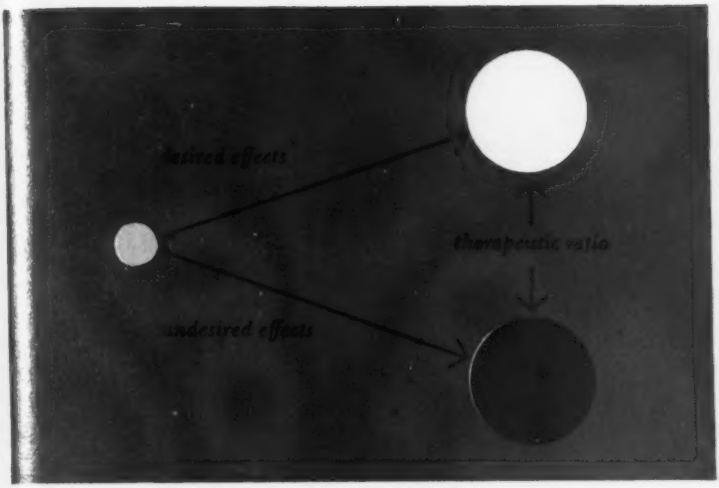
It has been demonstrated in a substantial series of cases that a buclizine-containing preparation markedly reduces the incidence of nausea and vomiting of pregnancy and is an effective prophylactic and therapeutic agent in this condition.[2] It was also observed that buclizine had definite tranquilizing properties, to more fully determine which this study of buclizine was conducted.

INDICATIONS

Patients in this group of 68 who received buclizine were being treated for such varied problems as menopausal syndrome, amenorrhea, habitual abortion, trichomonas vaginalis vaginitis, pruritus vulvae of specific and non-specific etiology, premenstrual tension, and other miscellaneous gynecological problems. In some of these patients where the main presenting problem was one which could be treated with a specific approach, this was also employed. In some conditions, on the other hand, the major presenting symptom (such as the menopause) was one which might be controlled by use of a tranquilizer

*Softran®, The Stuart Company, Pasadena, California.

1. P'an, S. Y., et al., *J. Am. Pharm. A. (Scient. Ed.)*, 43:653,1954.
2. Conklin, F. J. & Nesbitt, R. E. L. Jr., *Obst. & Gynec.*, 11:214,1958.



The best therapeutic ratio in the steroid field confirmed by a comparative clinical study of

prednisone
prednisolone
methylprednisolone
triamcinolone
dexamethasone

in 65 rheumatoid arthritis patients:

". . . It would appear from these comparative observations that methylprednisolone [Medrol] probably is the steroid of choice for initial trial in a patient with rheumatoid arthritis. It is potent, and displays a slightly improved 'safety' record, showing a reduced frequency of disturbing side effects compared with the other steroids."[1]

Medrol

TRADEMARK, REG. U.S. PAT. OFF. — METHYLPREDNISOLONE, UPJOHN

. . . hits the disease, but spares the patient

1. Neustadt, D. H.: Corticosteroid Therapy in Rheumatoid Arthritis: Comparative Study of Effects of Prednisone and Prednisolone, Methylprednisolone, Triamcinolone, and Dexamethasone, J.A.M.A., in press.

Upjohn

alone, and when this was the situation, buclizine alone was used.

DOSAGE

The dosage of buclizine was varied with individual patient sensitivity. Generally, patients were given one tablet every morning for one to eight weeks, then one tablet every morning and noon for one to eight weeks, then one tablet morning, noon and evening for one to eight weeks. In some instances, the dosage was increased to four, or on occasion, even eight tablets a day, to determine effectiveness or incidence of side reactions.

CONTROL STUDIES

To compare the effectiveness of buclizine in this group of 68 patients, two series of 50 control patients were each treated with other medications. One series was given aspirin and the other ¼ gr. phenobarbital according to the usual therapeutic schedule. Patients in all three groups were seen weekly when possible, and questioned as to degree of anxiety, irritability, unrest, insomnia, sensitivity to noises, etc. At these visits, weight, pulse and blood pressure were recorded for all groups.

LABORATORY DATA

Before buclizine therapy was started, complete blood studies, including white blood count with differential, red blood count, hemoglobin estimation, hematocrit, and sedimentation rate were made, together with routine urinalysis. In some cases repeat blood studies were done to better establish the norm for that patient. After administration of buclizine identical studies were done at intervals, in some cases almost weekly. In a substantial number of patients, the same laboratory tests were repeated several weeks after buclizine was discontinued. In all, some 600 laboratory studies were made.

TABLE I.

AGE INCIDENCE OF THIS SERIES OF 68 PATIENTS TAKING BUCLIZINE HYDROCHLORIDE

20 to 30	12
31 to 40	28
41 to 50	19
51 to 60	2
61 to 70	4
71 to 80	1
81 to 90	2
TOTAL	68

RESULTS

In the control group in which aspirin was employed, only 10 to 15 per cent experienced any degree of relief, with relative freedom from side effects. In the control group receiving phenobarbital in doses of ¼ gr. three to four times a day, 35 to 40 per cent said that they were less tense and felt generally better, but many of these complained of being sleepy and drowsy all day. They did not feel like working the next day and their minds were not clear. Some indicated that their visual acuity seemed somewhat dulled.

Of the 68 patients taking buclizine, 61 obtained results that could be classified as highly satisfactory. They became calmer, their fears, tensions, headaches and anxieties becoming so altered that they could now properly evaluate trifling things which previously had worried them a great deal. Most patients who experienced these satisfactory results were able to sleep all through the night without awakening, and the next day felt more capable of facing the duties and problems of everyday life. This change in emotional state was reflected in the office in their cooperation in keeping ap-

pointments and returning for further treatment. It has been the author's practice to interview these patients with some general type of questions like, "How do you feel? Worse, better or no change? Do you sleep worse, better, or notice any change in your sleeping habits?" It was very impressive to note how many of those taking buclizine replied to these questions with statements like, "I feel just fine" or "I feel much better."

The dose that seemed to be most generally satisfactory for our group of patients was one 50 mg. tablet three times a day, morning, noon and at bedtime, until symptoms were under control. This usually required four to seven days. Following this, the dose could be reduced according to requirements. Many could get along on one 50 mg. tablet a day, while others were instructed to take one on arising and one four or five hours later. The majority of patients could be maintained on a dosage of one or two 50 mg. tablets every 24 hours.

Patients who had initial normal blood studies and no intercurrent disorders maintained normal blood findings while on buclizine therapy. In addition, it was observed that even in an unusually high dosage such as 400 mg. a day, which was used on occasion, no significant side effects were noted. A few patients who took four to six tablets a day complained less of sleepiness than did those who took the more profound tranquilizers even in moderate dosage. Among patients who took one to three 50 mg. tablets daily, there were no side reactions of note.

A high degree of effectiveness and almost complete freedom from side reactions make buclizine a useful tranquilizing agent for the patient who leads an active existence, but is bothered by a variety of anxiety-type complaints associated with certain obstetrical and gynecological problems. This moderate-acting piperazine medication promotes the type of mental attitude that the physician likes to find in his patient when tranquilizing agents are employed. Buclizine is of marked value in those women who come to the obstetrician and gynecologist with fears, tensions, anxieties, and other mild neurotic disorders.

SUMMARY

1. Buclizine hydrochloride, a new tranquilizing agent, has been used in a variety of obstetrical and gynecological conditions associated with varying degrees of anxiety and tension. Sixty-eight patients were treated with the drug in doses ranging from 50 mg. to 400 mg. daily. Two groups of 50 control patients were also studied. One group received aspirin and the other received phenobarbital in doses of ¼ gr. three or four times a day.

2. Of the 68 patients receiving buclizine hydrochloride, 61 had therapeutic effects that were highly satisfactory with virtually no side reactions. Of the group of patients receiving aspirin, only 10 to 15 per cent reported significant therapeutic effect while in the group receiving ¼ gr. phenobarbital three or four times a day, improvement occurred in 35 to 40 per cent, but the incidence of side effects was relatively high.

3. Buclizine hydrochloride, in doses of 50 mg. three times a day for four to seven days, followed by maintenance therapy of 50 to 100 mg. a day, provides a highly satisfactory therapy of anxiety-tension states associated with many routine obstetrical and gynecological problems.◀

ORIGINAL ARTICLE

Psychiatric Emergencies and the General Practitioner

Immediate services from the general practitioner may be of far more benefit than delayed services from the most renowned specialist

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SUCH EMERGENCIES OF COMMON OCCURRENCE

Emergencies occur in psychiatry as they do in all fields of medicine. They confront the general practitioner and not infrequently demand urgent attention in the general hospital. In small communities and in rural areas where specialized psychiatric help is not readily available the responsibility for the early management of patients exhibiting acutely psychotic behavior falls directly upon the local doctor and the local hospital. No physician should lack the basic knowledge to meet this responsibility. It is his duty and his privilege to keep pace with modern therapeutic progress. He should, for example, be prepared to use the tranquilizing drugs, which, given in proper dosage intravenously or intramuscularly, are often highly effective in restoring the patient to a calmer state. Hospital psychiatric emergencies generally include violent delirious reactions, manias, assaults, attempts at suicide and excitements that sometimes occur in the course of acute or chronic brain syndromes. Elopements of disturbed patients are also regarded as emergencies.

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PROMPT PROPER MANAGEMENT DEMANDED

Prompt and efficacious management of the emergency depends upon the quick action of a well-trained team of doctors, nurses and aides. It also depends upon a previously prepared plan of action so that all resources of the hospital may be mobilized at once and fully utilized. Close liaison of the medical and surgical services and the ready availability of immediate measures for the treatment of serious emergencies, all the way up to suicidal efforts, are of prime importance. Formerly, restraints, seclusion rooms, hydrotherapy, large doses of barbiturates and narcotics were commonly used for disturbed patients. Nowadays the trend is toward less restraint and the judicious use of tranquilizing drugs and physiological shock treatments.

CAUSES ARE MANY

Delirium may be precipitated by alcohol, infections, toxins, drugs or head trauma. It is an acute brain syndrome characterized by great restlessness and by rapid shifts in the level of consciousness. It may appear gradually after a premonitory period of irritability and insomnia, or it may burst forth without warning. There is gross disorientation; misidentifications and misinterpretations occur; visual hallucinations are common, auditory hallucinations less so. Nightfall intensifies the symptoms. The predominant clinical picture may be that of the low muttering delirium found in typhoid or typhus fever, or it may be that of occupational delirium, or the symptoms may be unmistakably those of delirium tremens. The prevailing mood is one of apprehension, but at times, as may happen in delirium tremens, it is colored with amusement or grim humor. The disease is never static. Now the patient is lucid; now his mind is clouded and beset with illusions; now he is overcome with terrifying hallucinations, ready to leap from the window to escape from his pursuers. Delirium tremens usually runs its course in three to five days; the duration of other varieties depends upon the nature and severity of the causative condition. Fever, dehydration and exhaustion are common. Delirium is always serious and requires immediate treatment.

AND OFTEN MULTIPLE

Alcoholism and accidents unfortunately are often associated. Who has not heard of instances of delirium tremens where post mortem examination disclosed unsuspected subdural hematoma or contusion of the brain, or severe injury to abdominal viscera? Let the physician take heed and be ever on the alert that alcoholic delirium may obscure major effects of trauma. Nothing takes the place of keen observation and repeated, thorough physical examinations, with particular regard to the neurological status of the patient.

TREATMENT

The delirious patient should be placed in a quiet, darkened room. He should be closely watched and reassured frequently. An icecap to the head may be of help. Paraldehyde, still a favorite remedy, may be given by mouth in doses of 8 - 12 cc., repeated every four hours. Physical restraints should be applied only in case of dire necessity; wherever possible they should be avoided. The terror-stricken patient, victim of vivid hallucinatory fancies, will be

certain that his doom is sealed when he is tied down. Frantic struggling may reduce him to a critical state of exhaustion, and only coma and death may finally release him. The ataractic drugs are very useful in the treatment of delirious reactions. The cautious, intravenous administration of an ampule of 50 mg. of promazine* will result in remarkable abatement of the apprehension in a few minutes. The drug must be given slowly and frequently mixed with blood. In 15 to 30 minutes the dose may be repeated if necessary, and still later, 50 mg. of promazine may be given intramuscularly every four hours 'round the clock, depending upon the condition of the patient. Fluids and electrolytes must be supplied in adequate quantity. Intravenous infusions of 1,000 cc. of 10 per cent glucose in normal saline are useful for disturbed patients who are dehydrated and febrile. Thiamine chloride, 100 mg., may be added to the infusion. When the patient is able to eat, the diet should be rich in protein and supplemented with multivitamins. Daily injections of a vitamin B-complex preparation may be helpful.

BROMIDE DELIRIUM TO BE BORNE IN MIND

In those instances of delirium of obscure origin, bromide should be considered as a possible etiologic agent. Bromide delirium occurs more frequently than is commonly realized. If the diagnosis is suspected, the bromide blood level should be determined. If the diagnosis is established, treatment consists of forcing fluids by mouth and the administration of 2 - 4 Gm. of common table salt in enteric-coated capsules every four hours, or better, 5 - 7 Gm. of ammonium chloride per day in divided doses using enteric-coated tablets. The latter drug not only displaces the bromide ion but serves as a diuretic.

*Sparine®, Wyeth Laboratories, Philadelphia 1.

ETIOLOGIC DIAGNOSIS DIFFICULT IN MANY CASES

The general doctor may be called upon to give immediate treatment to patients who show violent behavior of one type or another. Manias may arise from manic-depressive psychosis, or as a feature of florid, catatonic excitement, often with great destructiveness. Murderous violence occasionally supervenes as a symptom of epileptic furor, or of acute pathological intoxication with alcohol. Transitory episodes of screaming and hyperactivity that sometimes occur in the course of chronic brain syndromes are less dangerous, but in no less urgent need of treatment.

VARIOUS TRANQUILIZING DRUGS

Here again, the tranquilizing agents have been of great benefit in calming and controlling these violently excited patients. Several of the derivatives of phenothiazine are available for parenteral use. Promazine may be used intravenously and intramuscularly. Prochlorperazine* may be equally effective; if this drug is used, 20 mg. (in ampules) may be given by deep intramuscular injection at once; in 30 minutes the dose may be repeated, and in four hours it may be given regularly every four hours by mouth or by intramuscular injection if deemed necessary. Perphenazine† is another effective remedy. This is prepared in 1 cc. ampules containing 5 mg. of the drug. One or two ampules may be

*_Compazine®_, Smith, Kline & French Laboratories, Philadelphia.
†_Trilafon®_, Schering Corporation, Bloomfield, N.J.

given immediately by the intramuscular route, repeated in a half hour, and then the drug may be continued in oral doses of 4 - 8 mg. every four hours depending upon the condition of the patient.

EPILEPTIC MANIFESTATIONS UNUSUAL IN NATURE

Epileptic phenomena such as fugues, furors, violent psychomotor equivalents and status epilepticus are real emergencies. Status epilepticus is a series of fits without recovery of consciousness in the intervals between fits. It is an exceedingly grave condition likely to terminate fatally unless the seizures are quickly stopped. Some authorities recommend the slow intravenous administration of 300 mg. of sodium phenobarbital; some prefer the rectal instillation of 1 to 2 Gm. of chloral hydrate in 25 per cent aqueous solution. If these measures fail, ether narcosis may be necessary.

BE ALERT TO PREVENT SUICIDE

Suicide ranks eleventh on the list of causes of death. Suicidal threats or preoccupations are to be taken seriously. Depressive reactions of all kinds, sudden changes in personality, withdrawal from interpersonal relations, should all excite suspicion. Postoperative and post-partum psychoses with strong depressive elements are common. The utter despair that grows out of chronic illness, hopeless malignancy and intractable pain may serve as a signal of impending attempts at suicide. Impulsive, unstable persons on one hand and severely schizoid, inhibited persons on the other are apt to be greater suicidal risks. Previous suicidal gestures or attempts should suggest that there may be repetition of these efforts. For the prevention of suicide no general rules can be given.

THE GENERAL PRACTITIONER CAN AND SHOULD BE QUALIFIED TO RENDER SUCH SERVICE

For the family doctor nothing is so important as sound judgment, ceaseless vigilance and a thorough knowledge of his patient. He represents the forward echelon of medical service. He has a proud tradition to uphold and it is heavily laden with responsibility. He upholds the standard of medical practice in his community. To be worthy of the name, he must possess a broad span of clinical knowledge; he must have good judgment; he must keep abreast of therapeutic advances. He must be resourceful, courageous and ready to respond to emergencies. What he does or does not do in these critical situations may determine whether the patient will live or die.

A brief summary of the more common psychiatric emergencies has been presented. The general doctor should be ready to meet these occurrences with the same confidnce and skill that he faces any medical or surgical emergency.◀

ORIGINAL ARTICLE

The Diagnosis and Treatment of Subclinical Bronchospasm

Subclinical status bronchospasticus is described, and recommendations are made for its diagnosis and treatment

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There is a group of asthmatic patients who are subclinically bronchospastic and therefore need special treatment, which often is not given to them.

These are not the occasional patients who wheeze only when exposed to specific food or inhalant allergens—pulmonary function studies often prove them to wheeze at no other time. Some of these as well as other non-allergic asthmatic patients may suffer from bronchospasm under circumstances as diverse as infections of any part of the respiratory tract, sudden exposure to cold water, swallowing cold foods or water, emotional storms, or effort. In many of these patients bronchospasm, indistinguishable from typical bronchial asthma, can be induced by having the subject either cough prolongedly or forcefully expire for a minute or more. In both groups however, and more frequently in the non-allergic asthmatic population, it can be demonstrated that there is some degree of bronchospasm continuously present. They are both subclinically and clinically bronchospastic, seeking help and taking medication intermittently only when the asthma becomes apparent and inter-

feres with normal activity.

It was observed that a percentage of patients suffering from nasal pollinosis became asthmatic. In an attempt to anticipate this deterioration, vital capacity determinations were done on a group of patients presenting themselves for the treatment of hay fever. Those in whom there was any history of asthma were excluded. It soon became apparent that during each pollen season, some patients demonstrated measurable diminution of total vital capacity, although some were not dyspneic and none were asthmatic. Over a period of five years, no straight-line relationship could be established between diminished vital capacity and the development of asthma. It was, therefore, erroneously concluded that diminished vital capacity and dyspnea were respectively a symptom and a sign of hay fever.[1] These observations have since been confirmed.[2]

Studies with 2,000 asthmatic patients indicate that this previously undescribed entity, subclinical status bronchospasticus, exists. A typical patient might complain of having suffered asthma in the not-too-recent-past and stethoscopic examination and roentgenograms might suggest a diagnosis of emphysema, since this may be present in mild or moderate degree. But timed vital capacity studies often show diminished expiration for each of the first three seconds of forced expiration prolonged beyond the third second with a total vital capacity sometimes equal to the predicated normal, but usually lower. Repetition of the studies proved the measurements to be constant.

Similar observations had been recorded previously.[3] A similar study concluded that pulmonary function may be impaired between attacks of bronchial asthma. The nature of the disturbance includes alterations in long volume and alveolo-respiratory function, as well as in ventilatory function, in which the greatest and most consistently encountered abnormality was present. It is possible that if such obstruction is kept at a minimum by adequate therapy, the high incidence of emphysema among bronchial asthmatic patients may be reduced. At the time of that paper, "adequate therapy" consisted of anti-allergic treatment and medicines taken as needed.

The sequelae of such subclinical bronchospasms have been delayed or prevented by injection treatment and continuous prophylactically-given anti-spasmodic and anti-inflammatory medications, combined as needed with antibiotic agents. Removal of secondary factors reduces the number of attacks suffered.

Psychotherapy is credited with improvement but rarely with "cures." It is true that these patients suffer fewer overt attacks of asthma, but there is little if any increase in timed vital capacity. The patient has learned to ignore or remain undisturbed by his organic lesion and perhaps to avoid some of the exacerbations due to emotional disturbances. But in many cases the inexorable long range process continues, and intercurrent infection or the development of emphysema is blamed for the recurrence of asthma.

Medical treatment for acute or chronic pulmonary infection, simple surgery, thoracic surgery for non-functioning lobes or localized bron-

1. Brown, E. A., *Dis. Chest*, 12:205,1946.
2. Goodwin, *Fed. Proc.*, 16:628,1957.
3. Lukas, J., *J. Allergy*, 22:5,1951.

chiectasis, will all result in fewer attacks.

That a large group of asthmatic patients are in a continuous state of bronchospasm can be established by the use of four groups of drugs used at first diagnostically (and excepting for epinephrine) now prescribed for continuous therapeutic effects.

In both children and adults, a demonstration that such subclinical bronchospasm exists can be obtained experimentally by the use of epinephrine 1:1,000 given subcutaneously in doses of 0.15-0.3 ml. This drug will not increase the vital capacity of normal non-bronchospastic subjects. In the patients under discussion, with lungs normal to the stethoscope but subnormal by the timed vitalometer readings, there is a temporary increase in all timed vital capacities as well as in the total capacity. It is not used routinely.

In a small number of patients, chiefly children and usually during the months from September to May, the use of potassium iodide alone, in initial doses of 0.15 gm. at intervals of two hours (with gradual extension of the time between doses so that the medication is taken on arising, mid-afternoon and at bedtime) will lessen the number of attacks of asthma or their severity. These patients are usually following programs for diminishing exposure to house dust and are often taking treatment by weekly aqueous or single annual or semi-annual repository emulsion injections. Those who follow the same program but do not take potassium iodide do not generally do as well in that the vital capacity does not increase.

Ephedrine will not increase the vital capacity of normal non-asthmatic patients, but in these subjects it will improve the vital and respiratory capacities and lessen the volume of residual air. It improves expiratory reserve volume. Used in conjunction with anti-allergic treatment and in doses of 50-60 mg. three or four times daily, it will, in patients in whom irreversible changes have not occurred, bring the vital capacity to the predicated normal. It is interesting that treatment of the allergy alone by elimination or injection programs will not often achieve as good a result.

Although when taken routinely the drugs improved the patients' vital capacities, they did not, in allergic or non-allergic bronchospastic patients, always take the vital capacity to the exact predicated normal level. It was thought that the patients' failure to improve further might be due to the irreversible changes caused by years of improper use or actual disuse of parts of the pulmonary system. The administration of steroid hormones to asymptomatic patients proved this conclusion to be false. Those patients who had reached the ultimate vital capacity provided by anti-spasmodic medication would often demonstrate a further increase when steroid hormones were prescribed in addition. Many of the 800 patients so studied reached the levels predicated for them. In the others the difference between the increased vital capacity and the predicated normal must, until further studies prove otherwise, be considered to be due to irreversible changes.

If further substantiation is needed that the basic hypothesis is true, the program can be reversed. The substitution of placebos or cessation of steroid therapy will be followed by a gradual decrease of the vital capacity to the levels achieved by the use of

feres with normal activity.

It was observed that a percentage of patients suffering from nasal pollinosis became asthmatic. In an attempt to anticipate this deterioration, vital capacity determinations were done on a group of patients presenting themselves for the treatment of hay fever. Those in whom there was any history of asthma were excluded. It soon became apparent that during each pollen season, some patients demonstrated measurable diminution of total vital capacity, although some were not dyspneic and none were asthmatic. Over a period of five years, no straight-line relationship could be established between diminished vital capacity and the development of asthma. It was, therefore, erroneously concluded that diminished vital capacity and dyspnea were respectively a symptom and a sign of hay fever.[1] These observations have since been confirmed.[2]

Studies with 2,000 asthmatic patients indicate that this previously undescribed entity, subclinical status bronchospasticus, exists. A typical patient might complain of having suffered asthma in the not-too-recent-past and stethoscopic examination and roentgenograms might suggest a diagnosis of emphysema, since this may be present in mild or moderate degree. But timed vital capacity studies often show diminished expiration for each of the first three seconds of forced expiration prolonged beyond the third second with a total vital capacity sometimes equal to the predicated normal, but usually lower. Repetition of the studies proved the measurements to be constant.

Similar observations had been recorded previously.[3] A similar study concluded that pulmonary function may be impaired between attacks of bronchial asthma. The nature of the disturbance includes alterations in long volume and alveolo-respiratory function, as well as in ventilatory function, in which the greatest and most consistently encountered abnormality was present. It is possible that if such obstruction is kept at a minimum by adequate therapy, the high incidence of emphysema among bronchial asthmatic patients may be reduced. At the time of that paper, "adequate therapy" consisted of anti-allergic treatment and medicines taken as needed.

The sequelae of such subclinical bronchospasms have been delayed or prevented by injection treatment and continuous prophylactically-given anti-spasmodic and anti-inflammatory medications, combined as needed with antibiotic agents. Removal of secondary factors reduces the number of attacks suffered.

Psychotherapy is credited with improvement but rarely with "cures." It is true that these patients suffer fewer overt attacks of asthma, but there is little if any increase in timed vital capacity. The patient has learned to ignore or remain undisturbed by his organic lesion and perhaps to avoid some of the exacerbations due to emotional disturbances. But in many cases the inexorable long range process continues, and intercurrent infection or the development of emphysema is blamed for the recurrence of asthma.

Medical treatment for acute or chronic pulmonary infection, sinus surgery, thoracic surgery for nonfunctioning lobes or localized bron-

1. Brown, E. A., *Dis. Chest*, 12:205,1946.
2. Goodwin, *Fed. Proc.*, 16:628,1957.
3. Lukas, J., *J. Allergy*, 22:5,1951.

chiectasis, will all result in fewer attacks.

That a large group of asthmatic patients are in a continuous state of bronchospasm can be established by the use of four groups of drugs used at first diagnostically (and excepting for epinephrine) now prescribed for continuous therapeutic effects.

In both children and adults, a demonstration that such subclinical bronchospasm exists can be obtained experimentally by the use of epinephrine 1:1,000 given subcutaneously in doses of 0.15-0.3 ml. This drug will not increase the vital capacity of normal non-bronchospastic subjects. In the patients under discussion, with lungs normal to the stethoscope but subnormal by the timed vitalometer readings, there is a temporary increase in all timed vital capacities as well as in the total capacity. It is not used routinely.

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If further substantiation is needed that the basic hypothesis is true, the program can be reversed. The substitution of placebos or cessation of steroid therapy will be followed by a gradual decrease of the vital capacity to the levels achieved by the use of

the anti-spasmodic drugs. Their replacement by placebos will often result in overt asthma corroborated by decreased timed vital capacity during, as well as between, attacks. The institution of steroid hormones alone will increase the vital capacity but the doses needed are larger than when they are given in conjunction with anti-spasmodic drugs.

These studies prove an overlapping of effects but no true congruency, although in many patients either the anti-spasmodic or the steroid drugs will bring the timed vital capacity to its predicated normal level.

Patients and sometimes physicians object to "taking pills all their lives." The same choice however, faces the patient suffering from hypothyroidism, Addisonian anemia, diabetes, hypertension and, in some patients, peptic ulcer. Once a patient has been convinced that his disorder is intermittently clinical but constantly subclinical, and that in time the subclinical illness can (and usually does) become more irreversibly clinical, there is no difficulty.

The basic disorder is a bronchospastic state. In allergic patients the elimination of causative allergens and the injection treatment for seasonal and non-eliminatable environmental allergens is mandatory. In the light of present knowledge, the prescription of medications to be used only for symptoms is not good practice.

The goal in the treatment of such subclinically bronchospastic patients is to reverse, decelerate or mitigate an otherwise inexorable process, and if possible to prevent the extension of the consequences of chronic pulmonary disease to other organs. The recognition of the fact that subclinical bronchospasm can be proved is the first step toward its successful treatment.◀

Abdominal Masses in Infants and Children

Since half of the palpable abdominal masses in infants and children are of urinary-tract origin, awareness of these entities is obligatory. These masses may be hydronephrosis, cystic disease of kidney, neoplasm, palpable bladder, results of trauma, congenital malformation, urachral cyst, horseshoe kidney, ectopic kidney, reduplication, solitary kidney of various shapes and position; perinephric of pelvic abscess. Congenital ureteral stricture is one of the most common causes of chronic pyuria.

Those of other origin may be retroperitoneal—neoplasm or infection, intraperitoneal neoplastic lesion, ovarian cyst, congenital malformation, pyloric stenosis, appendiceal abscess, splenomegaly, hepatomegaly, cyst—mesenteric, omental, or pancreatic.

The discovery, diagnosis and treatment of palpable abdominal masses in infants and children constitute a problem for all medical and some surgical specialists.

The kidney produces more palpable masses than any other abdominal organ in this age group.

The potential hazard of these lesions demands prompt, accurate diagnosis and appropriate therapy. Three-fourths may be correctly diagnosed by a careful history, physical examination, and a number of indicated laboratory tests.

Fetter, T. R., *West Virginia M.J.*, 55:48-54,1959.

CLINICAL NOTE

Successful Symptomatic Management of Dizziness, Vertigo and/or Meniere's Syndrome

Orphenadrine hydrochloride appears remarkably nontoxic and well tolerated, even by elderly patients, for symptomatic treatment of these disorders

J. WILLIAM FINCH, M.D., F.A.C.P., *Hobart, Oklahoma*

True Mèniére's disease is not frequently encountered in practice. In contrast, complaints of dizziness and vertigo (pseudo-Mèniére's syndrome) are made frequently, especially by older patients. Vertigo often occurs without warning after minor stress such as riding in a car, unusual situations, emotional upsets, etc. Heretofore, medical treatment of these patients has been rather unsatisfactory.

According to a recent report[1,2] orphenadrine hydrochloride* was found to be a safe and effective means of providing symptomatic relief in over 60 cases of Mèniére's syndrome. These results were similar to those observed in this study.

During a study of 100 patients with various types of skeletal muscle spasm, 11 of which had dizziness and vertigo as an important ancillary complaint,[3] orphenadrine hydrochloride was found to be an effective muscle relaxant. Of these 11 patients, seven were found to have Mèniére's syndrome, and four pseudo-Mèniére's syndrome.

The 11 patients included seven

*Disipal®, Riker Laboratories, Inc., Northridge, California.

1. Duursma, S., *Med. Times*, 86:573,1958.
2. Duursma, S., Report read at Conference on Neuropsychiatric Drugs, Amsterdam, Nov. 2, 1957.
3. Finch, J. W., *Clin. Med.*, 6:195-198,1959.

men, 32 to 103 years, and 4 women, aged 30 to 80 years. All were given the drug in a dosage of one tablet three times daily. Excellent relief from dizziness was obtained in six patients, good relief in four, no relief in one. Only one patient (with Mèniére's syndrome) complained of side actions. This was a man of 42 who reported that three tablets daily made him feel weak and faint. When the dosage was reduced to 2 tablets daily, the response was good, and there were no further side actions.

Two unusually interesting patients were brother and sister, aged 103 and 80 years, respectively. Both complained of severe vertigo and deafness (pseudo-Mèniére's). The sister had previously had only a fair response to ciphenhydramine hydrochloride. On orphenadrine hydrochloride, 3 tablets daily, both experienced dramatic relief from vertigo, with no side actions.

Orphenadrine hydrochloride has been used extensively as adjunctive therapy in parkinsonism, and it has been shown to have specific antispasmodic effects in skeletal muscle spasm.[4] Its action is essentially parasympatholytic, with unimportant antihistaminic effects. The pharmacodynamic mechanism in patients with dizziness is thus far unexplained, however, it is felt that the results obtained in this study warrant wider clinical trial and investigation by others.

CONCLUSIONS

Orphenadrine hydrochloride has proved to be a satisfactory mode of symptomatic treatment in 11 patients with vertigo, dizziness, and/or Mèniére's syndrome. It is remarkably nontoxic and well tolerated, even by very elderly patients. Results appear to be better than with other medications previously used.◀

4. Doshay, L. J., & Constable, K., *J.A.M.A.*, 163: 1352,1957.

Liquid Paraffin as a Cause of Oil Aspiration Pneumonia

An agent responsible for oil aspiration pneumonia in adults is liquid paraffin. It gains access to the lungs easily by its use as an ingredient in nasal or oral sprays. The evidence suggests that once in the lung, liquid paraffin remains as an inert foreign body for many years, perhaps permanently. Nose drops and sprays are now made up mostly in an aqueous medium, but about 20% are still in a medium containing liquid paraffin. Liquid paraffin gains access to the lungs as a result of oral administration, even in those who suffer no disability. It appears that there is still (in Great Britain) a steady sale for liquid paraffin as a laxative, and its use for this purpose requires reappraisal.

Oil granuloma of the lung is largely preventable. Its presence is known to dispose to recurrent respiratory infection, and in these days when our lungs have to contend with so many other noxious substances this is one lesion which we can well afford to be without.

Forbes, G., & Bradley, A., *Brit. M.J.*, 2:1566-1568, 1958.

Vicarious Liability for Medical Negligence

The same arguments making a hospital liable for negligence of staff members apply to negligence of the doctor's staff

M. A. MILLNER, B.A., LL.B. (Rand), B.C.L. (Oxon.),
Johannesburg, South Africa

The vicarious liability of a doctor or hospital in respect to staff or subordinates may be founded on breach of contract or delict (civil wrong).

BREACH OF CONTRACT

The relationship between a hospital or a doctor and a patient is normally a contractual one—the contract being for the rendering of medical services in return for a fee. Usually there is no writing, and no formal terms are discussed defining the extent of the hospital's or doctor's obligations. These are therefore left to be inferred upon the principles of the common law.

At common law, the parties are bound not only by the express terms of their agreement but also by implied terms. However, the court ought not to imply a term merely because it would be a reasonable term to include if the parties had thought about the matter. Neither should it be implied because one party, if he had thought about the matter, would not have made the contract unless the term was included. It must be such a necessary term that both parties must have intended that it should be a term of the contract, and have only not expressed it because its necessity was so obvious that it was taken for granted.

Thus if the patient relies on an

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COMFORTS • SOOTHES • RELIEVES CONGESTION

FOR 8 HOURS...AND MORE

The combined analgesic-decongestive medications in Numotizine act by steady and continuing infiltration from Numotizine's carefully formulated polyol-aluminum silicate base.

This slow release of comforting ingredients eliminates fussy care...allows patients to sleep without interruption all night long.

FORMULA: Guaiacol, 0.26%; Sol. Formaldehyde, 0.26%; Beechwood Creosote, 1.30%; Methyl Salicylate, 0.26%, in a kaolin-polyol base. Apply at least ⅛" thick over affected area, and cover with a suitable dressing.

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implied agreement to make the hospital or doctor liable to him for the negligence of a subordinate, he will need to show that it was a necessary term of the contract.

DELICT

Independently of contract, a man is generally answerable in law for injuries which he negligently causes to another. Negligence infers failure to exercise reasonable care. If a reasonable man would, in the circumstances, have foreseen the likelihood of harm and guarded against it, then the failure so to guard against that harm is negligence. If the harm materializes, the injured person is entitled to claim damages to compensate him for his injuries. Applied to a medical practitioner, this means that he is not expected to bring to bear upon the case entrusted to him the highest possible degree of professional skill, but he is bound to employ reasonable skill and care. In deciding what is reasonable, the court will have regard to the general level of skill and diligence possessed and exercised at the time by the members of the branch of the profession to which the practitioner belongs. Thus the law sets reasonable and not impossibly high standards of professional skill and care.

Ordinarily a man is only answerable for his own negligence in this way. However, the law recognizes the vicarious liability of an employer for the negligence of his employees, even though the employer is himself quite free from negligence and has exercised proper care in the selection of his employees for the task in hand. If a master-servant relationship exists between the hospital on the one hand and a doctor or nurse on the other, the hospital might be liable for the wrongdoing of that doctor or nurse on this principle. It will be seen, however, that the question of whether there is such a relationship of master and servant between the hospital and its subordinates, and, if so, to what extent, raises controversial problems.

LIABILITY OF HOSPITALS

A hospital contracts with its patients to use proper care in the selection of a competent staff and to place at the disposal of that staff fit and proper apparatus and appliances. If a patient were injured in consequence of the hospital's failure in any of these respects, he would plainly have a good cause for action—the hospital would itself be liable in respect of its own negligent conduct. But what if a fully competent member of the staff acts negligently towards a patient in a particular matter, thereby injuring him?

Ordinarily if X contracts to do something for Y and chooses to do it through his servants, he is answerable to Y for the negligence of his servants; that is implied in the contract. Similarly X is answerable to Y in delict for the negligence of X's servants. Nevertheless one English Court of Appeal refused to make a hospital liable to a patient who was negligently injured while under an anesthetic in the operating room. The patient was being examined by the consulting surgeon attached to the hospital, assisted by an anesthetist, nurses and aides. During the examination the patient's left arm came in contact with a hot water tin beneath the table and was injured thereby, and his right arm was bruised by pressure. Referring to the nurses and

aides, it was said that if and so long as they are bound to obey the orders of the defendants, it may be that they are their servants. But as soon as the door of the operating room has closed on them for the purpose of an operation they cease to be under the orders of the defendants and are at the disposal and at the sole orders of the operating surgeon until the whole operation has been completely finished. The surgeon is for the time being supreme and the defendants cannot interfere with or gainsay his orders.

In regard to the professional duties of its staff, a hospital escapes the liability which normally attaches to a contracting party who chooses to use servants for the performance of his contract. The fact that a servant is required to exercise professional skill does not, as a general rule, give rise to any such special implied term.

A patient, while recovering from an anesthetic after an operation in a hospital, was severely burned by a hot-water bottle owing to the negligence of a nurse. The court held that the placing of the bottle in the patient's bed and the subsequent supervision of him were professional duties on the part of the nurse, and that the hospital was therefore not liable. Decisions such as this appear to establish that a hospital is exempt from liability for the negligence of its doctors or nursing staff so long as that negligence was in the course of "professional" as opposed to "administrative" duties. It is not at all clear where administrative duties stop and professional duties begin; but virtually all a doctor's duties must surely be regarded as professional and most of a nurse's duties would be so too. Thus on this basis the injured patient's prospects of success in a law suit against the hospital would be slender indeed.

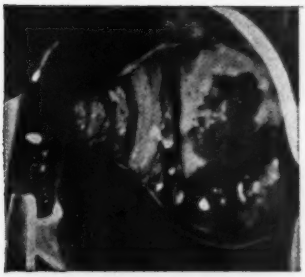
THE MASTER-SERVANT RELATIONSHIP

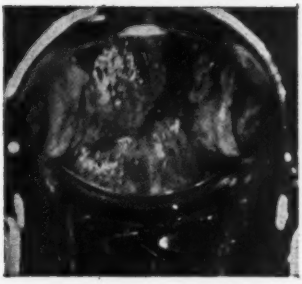
In the traditional view, a servant is one who is subject to the orders and control of his employer not only as to the work which he is to do but also as to the manner of doing it, as contrasted with an independent contractor, who uses his own discretion as to the manner of performance of the specified work. The argument that the mode of performance of professional duties is not susceptible to control has lost favor with the English courts. Recently an x-ray technician negligently failed to cover a patient's face with a lead-lined rubber cloth, with the result that the patient's face was permanently disfigured. The hospital was held liable.

DOCTOR'S LIABILITY TO PATIENT

A doctor is of course personally liable for his own negligence jointly and severally with the hospital that employs him. He would be liable also for acts done by subordinates, including nurses, in carrying out his own negligent instructions.

In one case the defendant was a surgeon who had performed an urgent and difficult abdominal operation upon the plaintiff, assisted by an anesthetist and a qualified surgical nurse on the hospital staff. One of the swabs was overlooked and remained in the patient's body. The evidence showed that, in accordance with the usual practice at that hospital, the surgeon had relied upon the nurse to count and check the swabs used and that at the end of the operation he had made as care-





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Candidiasis is especially serious in diabetics . . . during pregnancy . . . in the debilitated . . . and when broad spectrum antibiotics have been administered in high dosage, with or without concurrent administration of cortisone or related steroids.

Clinical Results. In 26 patients (11 pregnant) with vaginal moniliasis, treatment with Mycostatin Vaginal Tablets was completely successful in 92% of cases. Marked to moderate improvement was shown in the remainder.[2]

In a series of 59 patients with candidiasis (31 pregnant), intravaginal therapy with Mycostatin proved 100% successful in the pregnant patients; similar response was shown in 96.3% of the nonpregnant cases.[3]

Supplied. Each Mycostatin Vaginal Tablet—individually foil wrapped contains Mycostatin, 100,000 units, and lactose, 0.93 Gm. Packages of 15 with applicator. Also available: Mycostatin Oral Tablets . . . Ointment . . . Dusting Powder . . . Powder for Suspension . . . Cream.

References: 1. Lee, A. F., and Keifer, W.S.: Northwest Med. 53: 1227 (Dec.) 1954. • 2. Caruso, L.J.: New York J. Med. 58: 1688 (May 15) 1958. • 3. Pace, H. R., & Schantz, S.I.: J.A.M.A. 162: 268 (Sept. 22) 1956.

SQUIBB

Squibb Quality—the Priceless Ingredient

ful a search as the critical condition of the patient permitted.

The court held that the surgeon had not himself been negligent in the circumstances and that even assuming that the nurse had been negligent, the surgeon was not vicariously liable in respect thereof.

DOCTOR'S LIABILITY TO INDEMNIFY HOSPITAL

The servant is bound to exercise reasonable skill and care about his master's business, and the master is entitled to recover from the delinquent servant any damages which he may have to pay a third person in consequence of the servant's breach of this duty.

If the patient elects to claim from the hospital, the negligent person does not necessarily go free. Save where there is an implied understanding between them to the contrary (as may be the case when liability insurance is contemplated) he may yet have to answer to the hospital for what his negligence has cost it.◀

J. Forensic Med., 5:68-107,1958.

Progress in Ophthalmology

A malignant melanoma is to be suspected when any intraocular mass appears after age 40. It usually involves only one eye and spreads rapidly via the blood stream. It is composed of round or spindle cells and is commonly pigmented.

Using the radioactive P uptake test (P^{32}), a positive diagnosis of malignant melanoma often can be made. The tumor mass becomes very radioactive in comparison with the normal eye 24 hours after injection of the radioactive P. A drawback which is being studied is that the Geiger counter applicator is unable to localize tumor masses in the posterior pole of the eye.

The corticosteroids are being continually improved. The topical use of these agents combined with an antibiotic and used indiscriminately in unsuspected cases of virus herpes keratitis or *Pseudomonas pyocyanea* infections has caused loss of vision or even of the eye itself.

In the eye, topical corticosteroids alone or antibiotics alone should be used as indicated, and not the two in combination. The oral use of powerful antibiotics along with the corticosteroids often decides between sight and blindness.

A new oral aid in the treatment of glaucoma produces a marked lowering of intra-ocular pressure. A routine intra-ocular tension study on all patients past 40 years is suggested.

In retinal detachment some form of diathermy and buckling has jumped successes from 50% to 70 to 80%. For surgery of senile and juvenile cataract, the rate of success now is 93 to 97%. With the help of new drugs the most senile patient may have the benefit of cataract surgery under local anesthesia.

A plastic lens may now replace the cataractous lens. Corneal transplant technic has been simplified. Eye banks have been established in most states. The contact lens has been improved, most of the patients attesting to this wearing them the full day.

Esposito, A. C., *West Virginia M.J.*, 55:6-9,1959.

Comparison of Buffered and Unbuffered Acetylsalicylic Acid

A carefully controlled study seems to indicate that the "improved" aspirins offer no advantage over plain aspirin

ROBERT C. BATTERMAN, M.D., *New York, New York*

The analgesic effectiveness and gastrointestinal tolerance for a rapidly disintegrating unbuffered five grain tablet and a buffered five grain tablet that contained small amounts of dihydroxyaluminum aminoacetate and magnesium carbonate were supplied as identical-appearing tablets labeled "analgesic tablet C" and "analgesic tablet D." Both ambulatory and hospitalized patients were included. A total of 160 patients in four groups were given buffered or unbuffered drug, or both. The patients were taken from the medical, surgical and specialty wards of a hospital for acute and chronic diseases for the hospitalized patients, and the arthritis and medical clinics of two hospitals for ambulatory patients.

SHORT-TERM THERAPY

Seventy-six patients who attended the arthritis clinics for pain and disability from mild to severe degrees were treated. Selection was based entirely upon need for analgesics of the salicylate type. The patients were given either the plain or the buffered product on a random basis of alternate administration. All patients were to take two tablets (10 grains) every four hours for four doses daily.

They noted the effects of the dose in terms of degree of response, time required and duration of analgesia, and occurrence of gastrointestinal reactions.

Patients who had only one week of medication and failed to return were excluded. Those who stopped the medication during the first week of therapy because of gastrointestinal intolerance were included. The peak of effectiveness for both medications was at the first week.

Results for 40 patients compared by crossover testing under double-blind conditions also failed to reveal any difference between the two types of tablet. This held true for all groups studied—single dose, one week, or three weeks of therapy. The same effectiveness, regardless of analgesic satisfaction, was observed for both in 67.5 per cent of the patients for the initial dose. At the end of one week both medications had similar effects in 80 per cent. At the end of three weeks, results were similar in 62 per cent of the patients. Many patients noted the same intolerance for both preparations.

SINGLE-DOSE STUDIES

An attempt was made in another group of 22 patients to determine the validity of the patient's statements of effectiveness of the initial dose. These were given two tablets of either preparation by the double-blind technic, then observed for two hours. The results for the two types were the same and confirmed the information obtained in the previous group.

LONG-TERM THERAPY

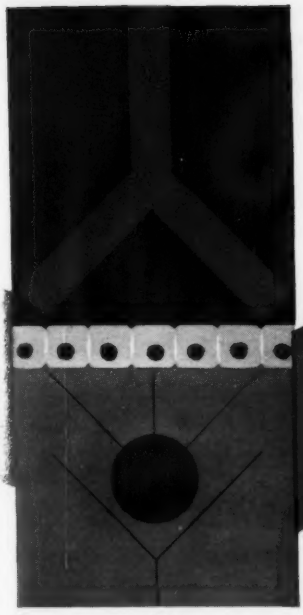
The previous study for three weeks may not have reflected fully the usefulness of such therapy for the long periods required by patients with arthritic pain. It was thought advisable to administer both medications for as long as nine weeks, 70 per cent of the trials lasting over five weeks. Two tablets were taken four times daily. The two types were found to be equally satisfactory for analgesic relief: 64.6 and 61.9 per cent respectively. Untoward gastrointestinal reactions occurred in 17.6 and 19 per cent respectively.

SINGLE-DAY COMPARISON

The same tablets with or without buffers were administered at random by the double-blind method to 56 hospitalized patients with a wide variety of medical and surgical conditions. The medication was two tablets four hours apart for four doses. After a day of either placebo or no therapy, the other medication was begun for a similar period of observation. In three cases pain did not occur during a trial of one of the medications, so that in these comparisons could be made only of tolerance. Satisfactory analgesia was the same for both types of tablets.

Crossover comparisons of analgesic response were possible in 53 subjects. The same effectiveness, regardless of degree of response, was noted in 40 of the 53 (76.4%). Five of the 18 patients not responding to acetylsalicylic acid noted analgesia with the buffered product; six of the 21 not responding to the buffered drug noted a satisfactory effect with the unbuffered product alone.

The frequency of gastrointestinal intolerance was also the same for the two preparations. This was noted in five patients (8.9%) for the unbuffered and in six (10%) for the buffered drug. Three patients were intolerant to both; two reported intolerance with the unbuffered but



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Dulcolax — in either tablet or suppository form — insures [illegible] effective bowel evacuation.

[illegible] exclusively by contact — [illegible] by systemic absorption.

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Is equally effective whether administered orally or by suppository.

Dosage: Tablets—1 to 3 (usually 2) at bedtime for bowel movement the following morning, or ½ hour before breakfast for a movement within six hours. Tablets are enteric coated, and must be taken whole, not chewed or crushed; they should not be taken with antacids. Suppositories—1 at the time a bowel movement is required.

Supplied: Dulcolax® (brand of bisacodyl). Yellow enteric-coated tablets of 5 mg. in boxes of 6 and bottles of 100. Suppositories of 10 mg. in boxes of 6. Under license from C. H. Boehringer Sohn, Ingelheim.

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Ardsley, New York

02659

not with the buffered product, and three noted intolerance to the buffered but not to the unbuffered preparation alone.

SPEED OF ABSORPTION

Different persons were used for each drug and for each interval of blood analysis. All were brought to a fasting and basal state and then were given two tablets, either with or without buffers. No differences were found between the two preparations in rates of absorption into the blood. The blood levels of either free or total salicylates at the different intervals were not modified by the form of the drug administered.

Another study was carried out using a crossover experimental design. Nine healthy young members of the laboratory or nursing staff in a fasting state were given two tablets equivalent to 10 grains of either the unbuffered or the buffered product. In the first week half received the unbuffered, half the buffered preparation. During the next week those who had taken the pure drug received the buffered product, and those who had taken the buffered preparation before received the acetylsalicylic acid alone. The addition of these buffers produced no significant difference in the rate of absorption of salicylate by these subjects for either the 10-minute or the 20-minute intervals.

THE INFLUENCE OF SODIUM BICARBONATE

Eight subjects were given 10 grains of acetylsalicylic acid and 20 grains of sodium bicarbonate. Free and total salicylate levels at 10 minutes were determined. An average level of free and total plasma salicylate was lower than that noted for acetylsalicylic acid alone.

SUMMARY AND CONCLUSIONS

A total of 160 patients was studied under several different clinical investigational conditions. The effects of a single dose, daily dose, short-term and long-term therapies were compared for unbuffered and buffered acetylsalicylic acid under conditions of double-blind technic, supplemented by crossover observations. In none of the four types of comparison used was it possible to distinguish between the medications for analgesic effectiveness or gastrointestinal tolerance.

The times required for analgesia, the degrees of analgesia and the frequency of gastrointestinal intolerance were identical for both preparations. A similar study utilizing the single-blind method produced the same conclusions.

Although sodium bicarbonate might delay the absorption of salicylate, the buffering antacids exemplified by aluminum compounds do not alter the rapidity of absorption of salicylate from the gastrointestinal tract of man.

Apparently antacids serve no useful purpose and their inclusion with acetylsalicylic acid offers no advantage over aspirin alone.◀

New England J. Med., 258:213-219,1958.

Functional Uterine Hemorrhage

A review of the etiology and treatment of functional uterine hemorrhage is presented

JOHN STALLWORTHY, F.R.C.S., *Oxford, England*

Such bleeding is due to imbalance of those hormonal and other factors normally controlling menstruation. It may occur either in association with, or in the absence of, organic pelvic disease. The clinical problem is that functional uterine bleeding may occur either in the presence or absence of ovulation, and from an endometrium that is histologically normal, hyperplastic, or even atrophic. Just as the ovarian response to gonadotrophins is not constant, so the endometrial reaction to ovarian stimulation varies.

DETERMINE THE CAUSE IN EACH CASE

From time to time women are seen with profound anemia after lengthy and expensive endocrine treatment for what was thought to be functional uterine hemorrhage, when an unsuspected submucous fibroid was the hidden enemy. In Britain probably more than in the United States another source of error sometimes revealed by the biopsy curette is endometrial tuberculosis, or even carcinoma of the corpus in a young woman. Even more important, because it is more frequent, is functional bleeding associated with anxiety states and emotional conflicts. Many a woman has been subjected to hysterectomy for recurring meno-metrorrhagia, when what she required was sensible contraceptive advice or guidance with an intimate problem which

the doctor ignored. Whatever method of treatment is favored for the syndrome, results will be unsatisfactory and may be disastrous without accurate diagnosis. A priest will sometimes render more help than a drughouse and treatment effective for metropathia could be disastrous for carcinoma.

HORMONE THERAPY

In busy practice neither the money nor the time necessary to establish a precise diagnosis before commencing treatment is always available. Endometrial biopsy or curettage should, as a rule, precede hormone therapy. Failing this, cervical cytology is an added precaution in a mature woman, but if for any reason the diagnosis is not established before treatment, hormones should not be administered more than an absolute maximum of three months without curettage, unless normal rhythm is restored and cytology studies are negative.. If puberty bleeding is not severe, one can temporize longer with safety, but the possible ill-effect of admitting a teenager to a hospital for curettage has to be weighed against the psychologic trauma of continuous or irregular bleeding. If the therapeutic response is not rapid, examination under anesthesia and curettage is necessary. When transfusion is necessary to replace blood loss in these young patients, the value of fresh, Rh-matched blood from a pregnant woman with its high hormone content should be considered.

TREATMENT

After repeated trials with both proprietory preparations and stronger solutions prepared for research, we have had no success in inducing ovulation by hormone therapy in the human..

Restoration of a more normal endometrial pattern with at least temporary relief of symptoms is usually much easier and there is no need to make it a complicated and expensive procedure. Estrogens are cheaper than progesterone, and in most cases cyclical estrogen therapy is effective. The theoretic need for both hormones correctly balanced is attractive, but it must be remembered that most women with anovulatory cycles menstruate regularly and apparently normally. The interaction of both hormones is obviously not a necessity. Moreover, the correct balance for the administration of estrogens and progesterone, even if both were necessary, is not known. In any series of cases of functional uterine bleeding there is at least a 50 per cent chance that ovulation is occurring with resultant progesterone influence of the endometrium. So-called physiologic curettage by progesterone administration is unsound and expensive unless easier methods have failed and biopsy has confirmed the metropathic picture.

STILBESTROL

A usually effective treatment plan, applicable in most cases, consists of giving stilbestrol 1 mg., or its equivalent, for 18 days commencing when bleeding ceases. It is then stopped until after the next episode of bleeding, when the same routine is repeated. This is continued for three months by which time, in a substantial proportion of patients, regular cycles are instituted. If the loss is continuous or heavy it may be curtailed by stilbestrol, 5 to 10 mg. daily. When bleeding ceases this dose is slowly reduced over a period of days to 1 mg., which is continued until the end of the 18 day interval. This simple routine

should not be continued for longer than three months, and if it fails curettage is indicated. In the event of recurrent irregularity the case should be assessed at consultant level. The use of pellet implantation or other forms of depot therapy are best reserved for the few cases in which simpler measures have failed and the endometrium has been studied histologically.

LIVER

Another valuable therapeutic weapon, not as widely known as it should be, is the administration of liver. Concentrated liver extract, 8 to 16 cc. daily, has been effective. In a series of 46 cases of functional uterine bleeding, the patients were given 2 capsules three times daily during active bleeding, and one to two capsules three times daily one week before a period for three months. No alternative treatment was given and 60 per cent of the patients were completely cured, 8 per cent materially improved. The shortest treatment given in this series lasted for two months, the longest for 10.5 months. The treatment was most effective in the younger groups, less so at the menopause. Nausea due to intolerance was rare. This preparation has been used with encouraging results; research is still in progress and it will be some time before detailed analyses are available. .

Reassurance is of great importance when no pathologic lesion is found. Anxiety can itself be a causal agent. Anemia must be treated but a practical point often overlooked is that some women lost more heavily when taking iron during a period. For this reason it is wise to stop taking iron on the eve of and during menstruation.

HYSTERECTOMY

In refractory cases, particularly at the menopause, surgery can restore the patient to health and activity while at the same time removing a real threat to her future. Curettage will restore 30 to 50 per cent to normal, at least temporarily, but if there is recurrence that fails to respond to cyclical hormone therapy we advise hysterectomy and usually perform it by the vaginal route.

Of 160 hysterectomies performed on women under 40 in the last five years, 83 (52%) were for functional bleeding which had not responded to the methods of treatment outlined.

Of 78 hysterectomies following a previous pelvic floor repair, 25 (32%) had the repair operation at 40 or over, and subsequently required a hysterectomy for bleeding. Of the total series, hysterectomy was performed on 25 for subsequent functional bleeding, and of these only two had the typical metropathic picture. Thirteen had non-secretory endometrium and 10 had a histologically normal secretory type. There were two cases of bleeding associated with thecomas.

When a pelvic floor repair is necessary in a woman of 40 or over, it is doubly important to carefully assess the whole clinical picture and if at that stage there is indication of functional bleeding, it is a wise plan to combine vaginal hysterectomy with the repair.

In a consecutive series of over 1,400 vaginal hysterectomies performed on women of all ages, including many poor surgical risks and women over 70, there has been one death. This was from cardiac failure on the third day after operation. Comparable results can be obtained

by the total abdominal operation, as shown by no operative deaths in 1,514 cases in the years 1951-1957. (There was one postoperative death from pulmonary embolism in a patient with heart disease.)

MAKE THE PATIENT SAFE FOR SURGERY

Surgery has been made safe for the patient and now the patient must be made safe for surgery. If this is attended to, the risk of major surgical procedures is now slight indeed. It should be remembered, moreover, that the dangers of carcinoma of the corpus developing in women with functional bleeding at 50 or over is increased, and for this reason there is a strong case against hormonal therapy and in favor of surgery for women in this category.◀

Northwest Med., 57:991-996,1958.

False-Positive Pregnancy Tests Caused by Tranquilizers

Positive results in the frog pregnancy test were produced by male as well as female patients who received these new drugs

GERARD H. HILBERT, M.D., *Pensacola, Florida*

During the past 10 years the use of the frog test for the diagnosis of pregnancy has become increasingly popular. In many areas it is now the only test used for this purpose. The main advantages of this test over the Friedman test are that quicker results can be obtained, the procedure is simpler, and the test animals are easier to handle and less expensive. False positive results have rarely been reported. One false positive finding, reported here, led to the investigation of this problem.

CASE HISTORY

A woman of 27 was admitted to the hospital with a clinical picture of an acute condition within the abdomen demanding immediate operation. Her complaints were cramping abdominal pains, vomiting and slight abdominal distention. She was not critically ill. On the second hospital day slight vaginal bleeding developed. A frog test performed on the fourth hospital day was reported as positive. The diagnosis of a ruptured ectopic pregnancy was entertained, and a laparotomy was performed. The operative and pathologic findings were a severe pelvic inflammatory disease with bilateral chronic salpingo-oophoritis and panhysterec-

tomy was performed. No evidence of pregnancy was found. On the fourth postoperative day, a frog test was repeated and again gave positive results.

In attempting to find out the cause of the false positive reactions, the patient's medications during her hospitalization were investigated and it was discovered that promazine hydrochloride was one of the few drugs she had continuously received. Specimens of urine of two other nonpregnant women receiving this drug were given the frog test, and both gave false positive results. Further studies consisted of the testing of specimens from 16 additional nonpregnant patients receiving the medication, and 11 receiving a similar phenothiazine compound. Out of the total of 30 frog tests, false positive reactions were obtained in 43 per cent—five in the 11 patients in the first group and eight in the 19 patients in the second group. Ten of the total tested were men. All of the patients were adults. On several of the patients, the frog test was repeated a few days after the drugs were discontinued, and the results became negative. The daily dosages of the drugs varied from 50 to several hundred mg. Direct injection of dilutions of these tranquilizing drugs into test animals failed to produce the emission of spermatozoa or a positive reaction.

Of three patients, serum specimens drawn on the same day that false positive tests were obtained on urine specimens failed to produce one positive reaction when injected into the test animals. Three of the urine specimens which produced false positive frog test results gave a negative reaction to the virgin doe rabbit (Friedman) test.

Patients receiving promozine hydrochloride gave a false positive reaction to the male frog test in 75 per cent of cases. The study included both male and female patients. Other false positive tests have been reported in recent years, but they are very few and are unexplained..

It appears that therapy with these drugs will produce in a significant number of patients a false positive reaction to the frog test for pregnancy when urine is used as the test material. The failure of serum specimens to produce a similarly false positive reaction to this test and the failure of urine specimens to produce a positive result in the Friedman test suggests that the substance producing the false positive result is an excretory by-product of these drugs. It is recommended that when a frog test for pregnancy is desired, serum be used in preference to urine as the test material when the patient is receiving a compound such as these.

In interpreting a laboratory report, the clinician should always keep in mind the possibility that newer drugs may interfere with various determinations.◀

J. Florida M.A., 45:955-957,1958.

Emergency Treatment of Thermal Burns of the Eyelids and Chemical Burns of the Eyes

Immediate first-aid treatment and careful medication and bandaging may prevent extensive sight loss

LLEWELLYN E. CHRISTENSEN, M.D., *Minneapolis, Minnesota*

To the importance of burns of the upper part of the face, by reason of danger to vision and to personal appearance, must be added that of the effect of the visual and cosmetic injuries on the emotional and economic status of the patient, his family and his community.

THERMAL BURNS

Thermal burns of the upper face usually involve the eyelids, but only about 12 per cent of patients with burns of the skin of the eyelids have burns of the eyeball. The eyeball is burned when flames or scalding material spread with explosive force, too fast for reflex closure of the lids, or when the heat is so intense or prolonged that parts or all of the lids are destroyed.

When burns of the face are extensive and endanger life, the important systemic treatment is usually the responsibility of the general surgeon and includes fluid replacement, control of pain and anxiety, maintenance of rest and body temperature, etc. Systemic use of antibiotics and antitetanus treatment are essential. Initial local treatment to the burned area is directed at the prevention of infection and restoration of an adequate covering as rapidly

The Menopausal Arthritic....

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REFERENCES: 1. Stein, I., and M. L. Beller, *Geriatrics*, 14:5 1959. 2. Howell, D. S., and C. Ragan, *Medicine*, 35:83, 19 3. Kammerer, W. H., *et al., Arth. and Rheum.*, 1:122, 19 4. Ward, L. E., *et al., Ann. Rheum. Dis.*, 17:145, 19 5. Banghart, H. E., *Amer. Prac.*, 5:964, 1954. 6. Pe W. H., *J. Phila. Gen. Hosp.*, 2:90, 1951.

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as possible to minimize resultant scarring and deformity.

First aid essentials are dry sterile dressing and systemic control of pain. When hospital care is obtained, the wound may be gently cleaned if extremely dirty (no vigorous cleaning, no debridement). Blebs are left intact as barriers against infection, and antibiotic ointments applied if gross contamination is certain. An initial layer of meshed gauze impregnated with petrolatum or boric acid ointment is placed over the wound, then a thick, tight fluff-gauze dressing is applied to make gentle compression and absorb the wound exudate. Such a dressing may necessitate complete envelopment of the head except for the nose and mouth. If the eyeball has not been damaged, an ointment may be applied to the eye and the eye left covered until the general dressing is changed.

The use of oils, oil-soaked cloths, or greasy materials is to be sternly discouraged in case of burns about the eyes, as for burns elsewhere. They are almost certain sources for contamination and make the later definitive wound treatment far more difficult. Picric acid, tannic acid, gentian violet, triple dye and the more recent plastic spray coverings have lost favor because of interference with new cell growth.

Burns are classified according to their depth as first degree (simple erythema, second degree (bled formation—partial destruction of skin with survival of some of the epithelial cells), and third degree (destruction of the full thickness of the skin).

In the partial-thickness burns where healing occurs from the surviving epithelial cells, antiseptics should not be used since they, too, interfere with cell growth. A suitable initial dressing protects from contamination and further injury. The deeper second degree burns heal with some scarring; the first degree and superficial second degree burns heal without scarring. In whole-thickness burns and some deep second degree burns, the convalescence is speeded up and the contractures and late deformities are minimized by skin grafting as early as possible. The most critical area for this early grafting is the skin of the eyelids.

Most thermal burns involving the eyeball show only mild erythema and require only a mild ointment and possibly atropine if the inflammation is marked. A pressure dressing usually makes for comfort and promotes healing. Small areas of more severe burns of the palpebral and bulbar conjunctiva and cornea are treated with lubricating ointments and repeated passage of a blunt probe along the fornix to prevent the formation of symblepharon.

Extensive deep burns of the conjunctiva are best treated by immediate mucous membrane graft. This graft may be conjunctiva from the other eye or buccal mucous membrane (lower lip or either side of the mouth). Buccal mucous membrane is not as satisfactory in an exposed area of the globe, as it remains permanently somewhat thickened and red. Deep burns involving the central cornea inevitably result in some degree of scarring and loss of vision. The use of cortisone cuts down irritability of the eye and reduces the density and vascularization of the scar.

CHEMICAL BURNS

A chemical burn of the eye results from local contact with a chem-

ical—solid, liquid, dust, mist, or vapor—of such degree as to alter the structure of the cornea and conjunctiva. Some alterations not visualized readily may be demonstrated by staining with 2 per cent solution of fluorescein.

Industries where this type of injury is particularly prevalent have adopted measures for prevention and have established facilities for first aid treatment. Any attempt to treat a chemical eye injury with a specific neutralizing material is now considered detrimental. The two exceptions to this rule are the treatment of lewisite burns with dimercaptopropanol and the commonly used cocaine hydrochloride for neutralizing the iodine used as a cauterizing agent in the treatment of dendritic (herpes simplex) infection of the corneal epithelium.

The treatment for all types of chemical eye injuries is the quick, thorough irrigation of the eye with water at the nearest source of supply, for five minutes. The patient should be immediately conducted to the physician, where after instillation of a local anesthetic, irrigation with water or normal saline is continued for half an hour. During this period the eye is carefully inspected, under loupe or slit-lamp magnification, and any insoluble particles on the ocular surfaces are removed using applicators or forceps. Gentle mechanical removal of injured or possibly contaminated tissue may be required. An antibiotic ointment is used to prevent infection and to provide lubrication in order to prevent adhesions. Use of local anesthetics is not continuous because of their detrimental effect on epithelial regeneration. A cycloplegic is indicated for any associated iritis, atropine for the more severe cases. Firm eye dressings give comfort, promote healing, and prevent mechanical disturbance of the regenerating epithelium. Use of cortisone reduces the inflammation, scarring and corneal vascularization, but should not be used in the presence of uncontrolled infection.

It is important to know the chemical nature of the substance causing the injury for predicting the probable course, prognosis and extent of treatment necessary. The action of acids of considerable strength is one of coagulation of all protein with which contact is made, forming insoluble acid proteinates—an instantaneous irreversible reaction. Penetration of the acid is limited by the barrier made by the dense layer of precipitated protein. A whole layer such as the cornea may be lost only when the injuring acid is great in concentration and amount.

Alkalies produce some of the most severe chemical eye injuries. The increase in hydroxyl ion concentration beyond the limits of tissue protein stability results in the formation of gel-like alkaline proteinates. In addition, alkalies combine with fats to form soaps and in this way they destroy the structure of the cell membranes and thus penetrate rapidly into the tissues. This speed of penetration is responsible for the capacity of alkalies to cause great intraocular damage.

Some other chemicals produce changes in the tissue proteins without altering the hydrogen ion concentration, which disable performance of its function and results in inflammatory and degenerative reactions. The injury to the eye from such a chemical may be just as severe as from alkalies and acids. Examples of these are the war gases, lewisite

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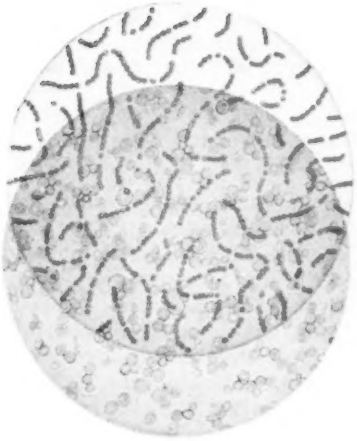

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Study of the chemical properties of the injuring substance is particularly important now that such a variety of products is being used in industry and the home, with new chemicals being added daily. When these properties are known we are aided in planning future treatment and predicting the prognosis of such injuries.◀

Minnesota Med., 41:5-7,1958.

Leg Blood Movement to Prevent Clots

When movement in leg muscles is reduced — as during surgery — the blood pools in the legs and conditions are set for the formation of blood clots. By keeping the patient "walking" through the electrical stimulation of the calf muscles, this pooling is reduced. The stimulation of the leg calf muscles causes the muscles to contract as they do in walking and to act as a pump forcing the blood back to the heart.

When the clots form, parts of them may break off and move through the vessels, eventually blocking the artery between the heart and lungs causing pulmonary embolism, now the commonest single cause of death following major surgical procedures.

Skin electrodes similar to those used in the study of the heart's electrical activity are used. The electrodes are placed on the legs and the closed electrical circuit produces regular contractions of the calf muscles during the operation and until the patient is conscious enough to move about.

McLachlin, J., et al., *New York J. Med.*, 59:657, 1959.

Indications for Lumbosacral Fusion

Fusion is indicated for patients over the age of 50 who have reoperation because of chronic low back pain

JOHN R. BLACK, M.D., *Los Angeles, California*

The first use of operations of this type was in cases of tuberculosis of the spine. Later they were used in scoliosis. In 1914 one surgeon performed a fusion of the lower back for relief of pain in that area and in 1929 he reported on 147 such cases. At that time, the prevalent theory as to the cause of low-back pain was that it was owing to mechanical defect, either postural or congenital. The indication for operation was severe or recurrent back pain not relieved by conservative measures, together with x-ray evidence of bony abnormality.

In 1932 fusion of both sacroiliac joints and fusion of the lumbar spine from the fourth lumbar vertebra to the sacrum was described. Some surgeons fused the spine from second lumbar to sacrum. In 1934 it was demonstrated that protrusion of a disc was a common cause of low back pain and sciatica and that it could be successfully treated by surgical means.

In 1940, surgeons began reporting more than one protrusion observed at the time of operation. Sometimes operation was done and no protrusion found. This was explained as "concealed disc" or "hypertrophied ligamentum flavum." It was noted that while removal of a classical protruded or ruptured disc brought about prompt and complete relief of sciatic pain, in other less typical cases oper-

ation did not bring relief.

LARGE SERIES OF CASES OF RUPTURED DISC

In 1941, a series of 193 cases of ruptured intervertebral disc were reported. In some of them spinal fusion was carried out in addition to removal of the protruded disc. The incidence of good results was 20 per cent higher in the group with fusion than in the group with laminectomy only.

Some surgeons remove the disc only, some use spinal fusion in all cases and some find a place for both operations. Clear-cut indications for each were still lacking.

In 1937, pseudarthrosis was found in 21 per cent of patients who had lumbosacral fusion and in 35.7 per cent of those who had spondylolisthesis. Others reported pseudarthrosis in seven per cent of cases in which fusion was done for ruptured lumbar disc; still others, 20 per cent with the note that with repeated operations the incidence of pseudoarthrosis increased.

MANY SURVEYS INCONCLUSIVE

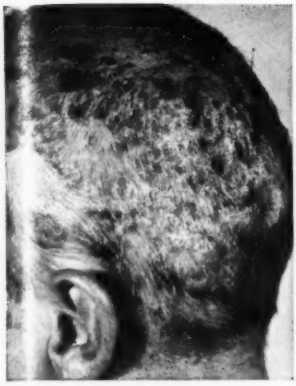
Many surveys made in an attempt to establish the role of congenital anomalies in low-back pain have been inconclusive, and in view of the proved role of disc degeneration and the increasing incidence of degeneration with advancing age, it appears no strong reason that these anomalies are incidental in the average case. It appears that once the disc is so degenerated or so damaged as to give rise to symptoms, the process is irreversible and attempts to correct faulty posture or poor body mechanics are probably useless.

Spondylolisthesis is considered a common cause of low-back pain. So long as the disc remains intact the relationship between the vertebral bodies remains the same, but when the disc degenerates slipping may occur, and degeneration symptoms are more likely. Evidence of disc degeneration was noted in 50 per cent of patients between 50 and 60 years of age, often without pain. The incidence of protrusion does not coincide with the increase in degeneration; the peak incidence of protrusion is between ages 30 and 40. In a young person with only one protruded disc and all other discs normal, fusion of the two vertebrae involved will result in an almost normal back. In patients past 60, severe pain in the back and legs with extensive degeneration of intervertebral discs who have removal of a protruded disc with or without fusion will manifest reduction of the pain in the legs, but complete relief of the back pain is not likely. We can never expect to return the patient to complete relief of back pain in any and all activities. The great majority of patients will return to work in spite of residual disability.

FOR AND AGAINST FUSION

If the patient has suffered from backache alone, the only procedure that could be expected to give satisfactory result is spinal fusion. In all cases in which there is sciatica, the spinal canal should be examined for nerve root compression. In all cases of protruded disc at the lumbosacral level where the spine above this level normal, spinal fusion should be done.

If the protruded or higher disc is at the level of the fifth lumbar interspace and there is evidence of at-



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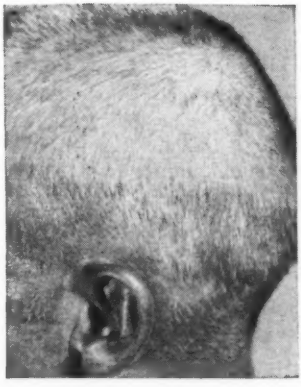

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trition of the disc or degenerative changes of the spine above, spinal fusion should not be carried out.

In cases in which reoperation is done because of persistent disabling back pain with or without sciatica, fusion of the affected area should be routine below age 50. In patients disabled by sciatic pain primarily, if sufficient pathologic findings are found to explain the pain and it can be relieved, fusion is not advisable.◀

California Med., 88:12-15,1958.

Plagues and Peoples

Despite all the marvels of medicine, it is possible that some muted or modified old disease, or some new entity, will arise and strike us a crippling or annihilating pandemic blow before medicine has found its cause, cure, or means of prevention. Witness the present Asian influenza epidemic. Had normal intercourse between Red China and the rest of the world not been curtailed, the disease would surely have had a more rapid and widespread effect. The means of communication and intercourse of the world's populations today is making all our diseases more cosmopolitan, and all epidemics to approach pandemic proportions. Along the lines of an old disease recurring, it has been interesting to read that oriental residents of this country for 30 or more years, and with no evidence of having the recent Asian type influenza, have shown serological evidence of past infection with this "new virus."

That diseases change in virulence is classically illustrated by the status of syphilis, changing from an endemic mild disease of the Americas to a fulminating and crippling disease that spread throughout Europe after Columbus' return. This disease followed a milder course among the whites after World War I, when the typical chancre of syphilis disappeared. Recall that tuberculosis, endemic in Europe for centuries, is far more virulent in the more newly civilized races, such as the Negro and Eskimo.

That as mild a disease as measles can decimate a virgin population is well attested by its introduction into the Fiji Islands. In 1875, when the King of the islands and his son returned from a visit to Sydney, they brought back the measles virus which in a previously uninfected population of 150,000 killed 40,000. Impetigo, a dread to mothers a score of years ago, seems now to have lost its virulence and recent experiments to spread the disease have met with surprising difficulty. Erysipelas is seldom seen and easily cured, but empyema has returned.

Many of our viruses and bacilli change their picture when passed through animals or humans, becoming more benign, *e.g.*, smallpox to cowpox and the tuberculosis bacillus to BCG; but others *e.g.*, the benign dermotrophic herpes simplex virus, become more virulent and neurotrophic when passed through laboratory animals. Again witness the many and ever-increasing neurotrophic viruses of today, such as those of poliomyelitis and the various encephalidites. Were they yesterday all just benign pharyngeal or GI invaders? What will they be tomorrow?

Allison, J. R., Jr., *The Recorder* (Columbia, S.C.), 25:28-36,1959.

Doctors and the Law

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CHARLES J. FRANKEL, M.D., LL.B., *Editor*

▶May a hospital, originally operated by a city and county, but now operated by a private corporation, refuse staff membership to doctors, solely because of color, if the city and county have a reversionary interest in the land on which the hospital stands and the hospital treats indigent patients under a contract with the county?◀

This question was passed on by a U.S. District Court in North Carolina in 1958 (*Eaton* vs *Board of Managers of the James Walker Memorial Hospital*, 164 F. Supp. 191). Pursuant to state statute, New Hanover County and Wilmington jointly built and operated a hospital. A resident's offer to build a new hospital was accepted; as a result the hospital corporation was chartered by the state legislature by a private law. The law's preamble stated that its purpose was to provide for the management of a hospital in the city and county to provide medical care for infirm poor persons where the city's and county's charity might be chargeable for such care and to provide care for other persons who might be admitted. The act further stated that its purpose was to remove the hospital's management as far as possible from the vissicitudes generally resulting when such an institution is controlled by local municipal authorities.

When the new hospital was completed, the city and county deeded the land on which it stood to the hospital

corporation to hold so long as it was used for a hospital for the county's and city's benefit; if the corporation ceases to use the land for this purpose it is to revert to the county and city. The deed stated that its purpose was to remove the hospital from problems resulting from political control. Since the conveyance of the land, the hospital has been operated solely by the hospital corporation, without interference by the city or county. Until 1951 there were state statutes providing for contributions by the city and county to the corporation; such states were declared unconstitutional in 1951. The corporation now derives no revenue from the city; it receives revenue from the county pursuant to a contract for the care of certified indigent patients.

Plaintiffs, negro doctors, applied for appointment to the hospital's "Courtesy Staff." It was admitted their applications were denied solely because of race. The present action was to compel their admission to the "Courtesy Staff."

The hospital contended that the denial of appointment was not "state action" and there was thus no federal jurisdiction. The Court said that the hospital corporation was not a public corporation simply because its purpose was to promote the public interest and convenience. Whether a corporation is public or private depends, not upon its purpose, but whether it is subject to the present control of public authority. The stated purpose of the statute creating the hospital corporation and of the conveyance of the land on which it stands was to remove it from political control. The only current governmental payments to the corporation are those by the county pursuant to the contract for the care of indigent patients. The past contributions of the city and the county to the corporation are not sufficient to make it a public one because they have no bearing on the present control of the hospital.

The only links to state control are the county's and city's reversionary interest in the land and the payments by the county under its contract with the corporation. These factors, said the Court, do not carry with them such control as to make the hospital a public corporation. The denial of the applications was therefore not "state action" and not a violation of the 14th Amendment.

►May a court disregard a doctor's alleged statement to his patient, which constitutes an admission of negligence, if such statement conflicts with known scientific facts?◄

This question was before the Supreme Court of North Carolina in *Kennedy* vs *Parrott,* 90 S.E. (2d) 754 (1956). During an appendectomy the doctor discovered some enlarged cysts on the patient's left ovary; he punctured them. The patient developed phlebitis in her leg. She testified that the doctor told her that when puncturing the cysts he cut a blood vessel and this caused the phlebitis.

The Court said that among doctors and others who made it their business to know human physiology, it is an accepted fact that phlebitis is caused by the inflammation of a vein and that it sometimes develops after an operation as a result of the anesthesia, operative shock and confinement to bed which, in combination, cause a slowing of the blood flow and dehydration of the blood, in turn producing inflammation and the forma-

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References: 1. Sheldon, J. M.: Postgrad. Med. 14:465 (Dec.) 1953. 2. Hubbard, T. F. and Berger, A. J.: Annals Allergy p. 350 (May-June) 1950. 3. Kline, B. S.: J. Allergy 19:19 (Jan.) 1948. 4. Goodman, L. S. and Gilman, A.: Pharmacol. Basis Ther., Macmillan, New York, 1956, p. 532. 5. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 6. Lhotka, F. M.: Illinois M.J. 112:259 (Dec.) 1957. 7. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958.

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tion of blood clots. The textbook statements about phlebitis were corroborated by the doctor's expert witnesses. They testified that if the doctor made the statement attributed to him, he was wrong and that the phlebitis was caused by the anesthesia, surgery and bed confinement. Even if it is assumed that the doctor made the statement attributed to him, it is so in conflict with the known scientific facts as to lack sufficient probative force to warrant its submission to the jury.

►Is a doctor who certified on a doctor's service report filed with a hospitalization insurance company that he personally provided the services for which payment was requested, guilty of obtaining money by false pretenses where part of such services were performed by a chiropodist in a hospital operated by the doctor?◄

This question was answered by the Superior Court of Pennsylvania in 1958 (*Commonwealth* vs *Litman*, 144 A. (2d) 592). The space on the form for the description of service provided had the following heading: "Report Only the Service You Personally Rendered the Patient." Below this was the following certificate: "I certify that I was the doctor in charge of the patient during the period shown above and that I am legally qualified to perform the service stated herein and that I personally provided said service." The doctor left blank the space calling for the name of any other doctor who participated in the case. The reports allegedly containing false representations related to cases in which part of the service rendered was minor surgery performed by a chiropodist. The surgery was performed in the hospital owned and operated by the doctor. The doctor was not always present when the operations were performed but he was at all times available in a supervisory and consultative capacity. The doctor furnished pre- and post-operative care to the patients.

The Court said the doctor did not misrepresent facts in his service report. He certified merely that he personally provided the services to the patient. In order to provide the services he did not have to personally perform the operations. Leaving blank the space relating to other doctors participating in the case was not a misstatement of fact. He was the doctor in charge and no other doctor was present. He was available to furnish a doctor's services if an emergency arose and he did furnish pre- and post-operative care.

The Court further said it did not perceive that anybody was defrauded of anything. The insured received the service for which he paid and the insurer paid for the service the exact amount it agreed to pay. It is immaterial that the insurer is prohibited by statute from making direct payment to a chiropodist for such service. Payment was not made to the chiropodist; it was made to a qualified doctor who was in charge of the case and who provided the service. The doctor was therefore not guilty.

►Is the doctrine of res ipsa loquitur applicable to a malpractice action based on sciatic nerve injury following a hypodermic injection in the patient's buttock?◄

This issue was before the New Jersey Superior Court, Appellate Division, in 1958 (*Toy* vs *Rickert*, 146 A. (2d) 510). In treating the patient's cold, the doctor administered a prolonged-acting penicillin preparation into the patient's right buttock by hypodermic injection. Within ten sec-

onds the patient's right leg from the thigh to the foot became numb. The leg's insensitivity subsided in two weeks but was followed by extreme pain in his foot. The pain in the foot abated in eight months but the patient still has a dull ache and walks with a slight limp. There was expert testimony that the pain was caused by osteoporosis of the bones of the foot resulting from sciatic nerve injury.

The patient contended that the doctrine of res ipsa loquitur was applicable. The Court said that, although there was no reported medical malpractice case in the state in which the doctrine had been applied, there was no reason not to apply the doctrine to such cases, provided the plaintiff satisfies its requirements. The first of these requirements is that laymen, as a matter of common knowledge or experience, could infer that the injury would not have occurred if proper care had been exercised. This requirement has not been satisfied here. There are many variables and imponderables concerning hypodermic injections which are not within the common knowledge and experience of laymen. A layman could properly infer that the injury might have resulted even though the doctor exercised ordinary professional care.

►May a court-appointed panel of psychiatrists testify as to the results of their examination of the defendant when that examination was guided by information obtained by one of them when he was acting as the defendant's personal psychiatrist? Did the defendant waive the doctor-patient privilege when he failed to object to the panel's membership when it was appointed?◄

These questions were passed on by the Supreme Court of Michigan in *People* vs *Wasker*, 91 N.W. (2d) 866 (1958). The defendant was charged with the crime of gross indecency. At the request of the prosecutor, the court appointed a panel of three psychiatrists to examine defendant to determine whether he was a criminal sexual psychopathic person. Defendant had conulsted one of those appointed as a private patient following his arrest. Defendant made no objection to this psychiatrist's appointment to the panel until the hearing on the panel's report when the jury found defendant to be a criminal sexual psychopathic person.

The prosecution admitted that the panel member who had treated defendant privately made extensive use of notes and hospital records compiled during that treatment. The Court said that, although it could not determine the precise extent to which this information influenced the panel, it was probably largely determinative of its final opinion. The report was necessarily tainted by the information gained in the course of the confidential relationship.

The prosecution contended the defendant waived the doctor-patient privilege by failing to object prior to the hearing on his psychiatric status; it was claimed that the failure to object earlier was a trap. The Court said the prosecution's claim it had been trapped was not a satisfactory answer to defendant's claim that his rights had been violated. Defendant was under no obligation, prior to the hearing, to object to the appointment of a panel of psychiatrists, and his objection at the hearing to the psychiatrists' testimony, because it was, of necessity, based in part on confidential communications, was therefore timely.

EDITOR'S NOTE: Many states have ruled contrary.

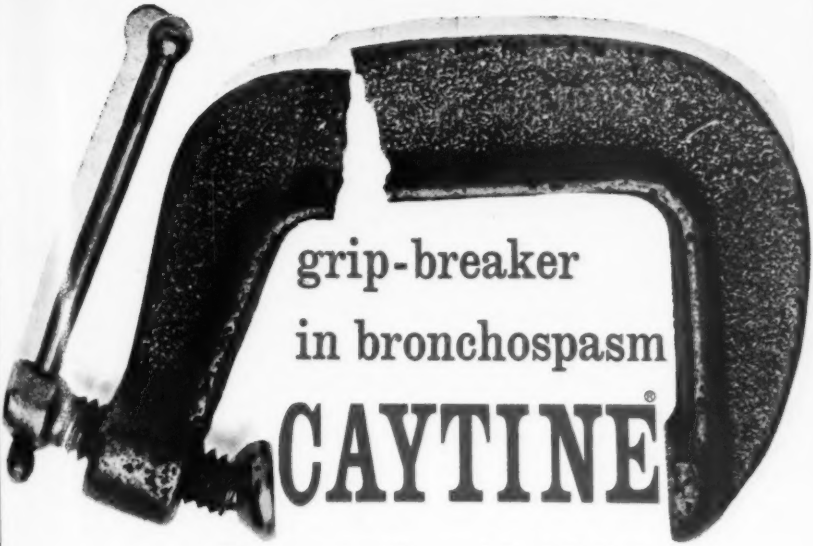
►Can a patient claim the doctor-patient privilege even though he did not himself hire the doctor?◄

This question was presented to the New York Supreme Court in 1955 by a rather unusual set of facts (*Jones* vs *Jones*, 141 N.Y.S. (2d) 820). This was an action by a husband for the annulment of his marriage on the ground that his wife had fraudulently concealed she was pregnant by another at the time of marriage. The marriage occurred September 12, 1953; a child was born April 25, 1954. The wife defaulted and a guardian was appointed to represent the child's interests in the action. The husband sought to ask questions of the doctor, who attended the wife through pregnancy, as to the child's weight and general physical condition at birth and as to any indications whether the child was full-term or premature in order to establish the time of conception. The guardian's objections to the questions were sustained. The Court said the mother may have waived the privilege by defaulting but the child could claim the privilege because the doctor also professionally treated her. It does not matter that the doctor could not be directly engaged by the child, when a viable foetus or when later born. The privilege exists whether the doctor was called in by the patient or by another and it is immaterial that the patient was unconscious or unaware of his presence. The test is whether the doctor gives professional treatment for the patient's benefit.

►What constitutes knowledge of malpractice which will cause the statute of limitations to begin to run? Does it make any difference that, although there is knowledge of the malpractice, there is no knowledge of the permanent nature of the injury caused thereby?◄

A California District Court of Appeal passed on these questions in *Calvin* vs *Thayer*, 310 P. 2d) 59 (1957). Shortly after being injured in an automobile accident in June, 1952, the patient engaged defendant doctor's services. Throughout the course of treatment the patient suffered from extreme pain in her head, dizziness, nausea and impairment of vision; defendant attributed this condition to ailments from which she had previously suffered. The doctor-patient relation was terminated January 6, 1953. She then consulted Dr. Seletz who informed her on January 9 that there was an increased pressure within her head due to a head injury and that he feared surgical treatment might be required. On January 17, the patient entered a hospital for an air study and surgery, if indicated. At this time, the patient signed a paper which stated, over Dr. Seletz's signature, a preoperative diagnosis of "possible Subdural Hematoma." On January 19, the patient signed a paper which read in part: "Operation and anesthetic record . . . preoperative diagnosis, shaving of head." The patient filed this action on January 28, 1954.

Defendant contended that action was barred by the one year statute of limitations. The plaintiff argued the action was not barred because the evidence was insufficent to sustain a finding that she had knowledge of the facts giving rise to her cause of action more than a year prior to filing her action. The Court said the information given the patient by Dr. Seletz before and after the operation was such that she must have known



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(1) Leslie, A., and Simmons, D. H.: Am. J. M. Sc. *234*:321, 1957. (2) Settel, E.: Am. Pract. & Digest Treat. *8*:1249, 1957.

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the facts constituting her cause of action. He made it clear to her on January 19 and 20 that defendant had made an incorrect diagnosis and not given her condition the care it required. The statute began to run when she acquired this knowledge. Since the doctor-patient relation had been terminated prior to that time and defendant did nothing thereafter to stop the running of the statute, the action is barred.

The patient further argued that, although she knew of defendant's malpractice more than a year prior to filing suit, she believed that it had caused only temporary injury, and she only learned her injuries were permanent within one year prior to filing suit and there was thus a cause of action for permanent injuries that was not barred. The Court said this argument had no basis in reason or authority. The patient had a single cause of action for her damages and, if there had been any recovery, it would have included compensation for damages sustained to the time of trial and also for future damages that could be shown to be the reasonably probable consequence of the injury.◀

FINANCE

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

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These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many business men. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

Recognition of changes of various various kinds in companies is frequently among the most important factors in a successful investment program. The investor who becomes aware of fundamental changes in the nature of a company's operations early enough is often well rewarded. Over the past few years, many such changes have taken place. Probably the most dramatic were those in Lorillard, the cigarette firm, and American Motors, producer of the Rambler. Investors who realized the huge potentials of Lorillard's Kent cigarettes and American's Rambler saw their investments increase four-fold in a two-year period.

This month, four issues where ba-

sic changes of differing types are taking place will be discussed. While less dramatic than the huge improvements wrought for the two above-mentioned firms, all are believed to be important to the companies concerned, and will increase the value of the shares involved.

The first, Martin Co., is gradually evolving from an aircraft company to a scientific supplier to the government, placing growing stress on electronics. The second, Walworth Co., a leading producer of valves and fittings, is now in the midst of a drastic reorganization of its physical productive facilities, digesting several corporate acquisitions of recent years and spending growing sums on research. The third, Flintkote Co., a diversified building products company, is growing to national status in such products as cement and gypsum. The fourth, Anaconda Co., is bringing a huge new copper mine in Chile into production and will thus substantially increase its basic earning power.

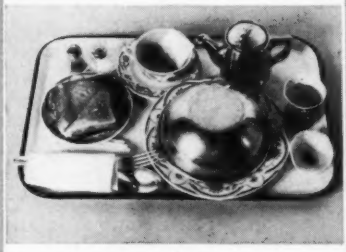
THE MARTIN COMPANY

Martin Company has had a considerable improvement in its position in recent years, which is now becoming especially noticeable as the result of the company's concentrated efforts on diversification of products and customers, particularly in new and growing fields. For all practical purposes, Martin can be described as a supplier to the Government, servicing all the military branches as well as some scientific areas. Sales and earnings are trending upward, and contracts are beginning to shift over to the more profitable fixed-price type. Further significant improvements in this situation are expected, although of course the shares must be regarded as quite speculative because of the nature of the company's activities and its heavy dependence on Government spending.

Martin has returned from the brink of bankruptcy to become a prosperous organization that is becoming one of the most important factors in the missile program. In addition, the company's electronic capabilities have been greatly expanded, adding to the integration of the operation, as well as providing profitable employment of facilities previously used for other purposes. A large part of the credit for the recovery in the Martin picture must be attributed to top management, which was brought in 7 years ago when the company sustained heavy losses on commercial transport planes.

At the present time, Martin's largest single activity is the Titan intercontinental ballistic missile built for the Air Force. The Titan is a two-stage missile that appears to have great capabilities for carrying a large payload over longer distances than any of the other ICBM's. Just three years ago the company broke ground for a new facility in Denver, Colorado for the manufacture and static testing of this weapon. Although the Titan manufacturing facilities are not yet fully completed, the company has a production line for it, a test cell building for checking out the electronic and other components and four huge test stands for static testing of the propulsion systems. The Denver facility is very well integrated. Full check-out and testing are major factors in the great success achieved in the launching attempts of the Titan missile to date, four out of four being completed in a space of less than 3 months.

At Orlando, Florida, Martin has just completed a new plant which



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produces the LaCrosse, Bull Pup, and Pershing missiles, as well as an electronic brain, the Martin Missile Master. Although the LaCrosse surface-to-surface missile is for the U.S. Army, it is also being considered by the Marines, Canada and NATO Forces. While of relatively short range the LaCrosse is capable of carrying either a conventional or nuclear war-head, and is zeroed-in to its target by electronic controls from advanced field positions. Currently being turned out on cost plus-fixed-fee contracts, it is expected to go on a fixed-price basis some time next year.

The Bull Pup tactical missile is for the Navy, and is already operational on planes on the aircraft carrier Lexington. The Air Force is considering the missile, with slight modifications, which would probably be known as White Lance. These missiles are of the tactical type for air-to-surface utilization against specific targets.

Much more highly classified is the Pershing two stage solid propellant missile which is a modification of the liquid propelled Redstone Missile. Martin is working very closely with subcontractors on the Pershing, which is expected to become an important weapon in the nation's missile arsenal. It is designed primarily for army utilization.

The company's huge Baltimore facilities still turn out P5-M-2's for anti-submarine work, and have also been used to produce a number of jet propelled P6M Sea Master flying boats. Martin also does some subcontract work at Baltimore, but in general is gradually phasing out of aircraft production and placing greater reliance on missiles and electronics. The Baltimore plant is now the manufacturing center for the Mace tactical missile for which Martin has just been awarded additional follow-on orders.

The Martin Missile Master electronic system, for the integration of intercepter planes and anti-aircraft missiles, defends a given sector. The original installation is at Fort Meade, Maryland, and other installations are being made to protect major cities. A highly complex electronic unit, the Missile Master is capable of tracking and computing all flying objects in a given area, and of sorting out friend from foe. It is also able to direct specific planes or missiles against selected targets. Obviously, this installation represents a highly complex electronic capability including very high speed computers and similar devices.

Martin's scientific achievements include the Viking and Vanguard rockets. The latter is a highly scientific instrument which has placed two satellites into orbit, both of which are expected to far out-live the military-type casings, since the orbit was more carefully calculated to return scientific data. This careful scheduling, plus the high degree of instrumentation, accounts for some of the early delays in reaching orbit.

For the longer-term future, Martin is undertaking highly extensive research studies into a great many fields, including mathematics, the biosciences, solid state physics, chemistry, and metallurgy. The company is also competing for new military and scientific projects, most important of which is the space glider, Dyna-Soar.

Management has been considerably strengthened by many young, capable and aggressive people. Chief interest in the Martin situation lies in future potentials by reason of its research activities in new and growing fields. Also, as it becomes more generally recognized that Martin is becoming

THE MARTIN COMPANY

Price	$58
Dividend	$1.60
Yield	2.8%
1959 Price Range	62¾-32⅜
Where Traded	N.Y.S.E.

Capitalization (12/31/58)	
Long-term debt	$20,000,000
Common stock	2,924,877 shs.

essentially an electronics producer, the shares may well be afforded a much greater price-earnings ratio than currently prevails.

Earnings this year are presently estimated at about $4.50 a share on the present number of outstanding shares. There may be some dilution, however, either by exercise of warrants or issuance of additional shares for acquisitions, since the company is determined to penetrate still further into its chosen fields and is aiming for a high degree of integration. Such earnings would compare with $4.01 a share in 1958 and $3.38 a share in 1957.

WALWORTH COMPANY

Walworth Company is the second largest producer of valves and fittings, which are sold to a wide range of industries. Roughly half of sales go to replacement of wornout equipment, while the balance depends on the level of capital expenditures. The expansion in sales of recent years is due both to acquisitions made in 1955-56, and to a general increase in business. Since the industry is competitive, margins have been volatile.

Several years ago, in an attempt to improve its position in the industry, Walworth decided to broaden its line by acquiring fast-growing, well-managed and highly profitable companies in the same field. The next two steps are presently being carried out. One involves the drastic reorganization of the parent company's manufacturing operations, which began in 1958. The other looks to the long-term, and has resulted in a change in sales philosophy and greater emphasis on research. Last year, a new research engineering building was completed.

Five companies were acquired in 1955 and 1956. M & H Valve Fittings, which sells valves and hydrants for water distribution, filtration, sewage disposal and fire protection was the first. Alloy Steel Products sells a complete line of stainless steel and other corrosion resisting valves in the chemical, drug and food industries. It is the largest factor in this highly technical field. Southwest Fabricating and Welding forms or fabricates pipe for new installations of oil refineries, gas pipelines and power plants. Grove Valve & Regulator sells a specialized gate valve, mostly to the oil industry. It also produces automatic pressure regulators for public utilities. Finally, Conoflow Corporation sells automatic control devices to process industries.

Last year, the subsidiaries are understood to have earned more than $4 million before taxes. On a consolidated basis, however, Walworth reported a net of only $2 million pre-tax, indicating a loss for the parent company that year. The main problem has thus been the earning power of the parent company which lost around $2 million pre-tax in 1958. This resulted from very low margins plus the cost of the unusual steps taken in 1958 to reorganize production.

WALWORTH COMPANY

Price	$17½	Capitalization (12/31/58)	
Dividend	*	Notes	$15.2 million
Yield		Common stock	2,211,176 shs.
1959 Price Range	17¾-12½		
Traded	N.Y.S.E.		

*2% stock paid February 1959

It is estimated that 60% of the production of the parent company is being reorganized, which will lead to economies of labor. Furthermore, when the project is completed in the latter part of this year, costs should be appreciably smaller. A chief factor is the new Braintree, Massachusetts plant, which will consolidate the bronze valve operations of three former locations. In 1958, extraordinary costs associated with this move came to $1.2 million. There will be additional special costs during the first three-quarters of 1959, but when all is completed annual savings of $3.5 million pre-tax are anticipated.

In 1958, the nationwide drop in capital expenditures led to a sales decline for Walworth to $77 million, from the $95 million of the year before. Since prices were off sharply, the physical volume of shipments fell less than the drop in sales. As a result, 1958 earnings per common share were only $0.37 against the record $2.31 in 1957. As mentioned above, net income was charged with extraordinary plant reorganization costs, which came to $0.54 a share.

This year a marked improvement is expected. Initially, however, continuing extraordinarily heavy expenses will probably result in a deficit for the first half of 1959. In the fourth quarter, however, efficiencies achieved are expected to lead to earnings of at least $0.70 per share. Because of the importance of special costs, it is not feasible to estimate earnings for the full year 1959. The last quarter's rate is expected to continue into 1960, and improve further with recovery in sales so that at least $3.00 for that year is estimated.

Early in 1958 the quarterly dividend was 30¢. This was reduced to 15¢ quarterly, and finally omitted entirely while a 2% stock dividend was paid in February 1959. With recovery in earnings next year, and the completion of the expansion program, restitution of quarterly payments is expected. Late last year, there was an internal dispute over control. Several months ago this was settled, however, with greater representation on the Board of Directors granted the former insurgents.

Walworth is thus recommended as an attractive issue for intermediate term gain. Current and recent earnings are not considered representative since the company is on the verge of a major surge in earnings. This improvement, expected primarily from the reorganization of physical plant, a step-up in capital expenditures by industry and firming prices for the company's products, should result in earnings of $3.00 or better in 1960. Accordingly, at present prices the shares under-valued and the downside risk appears moderate.

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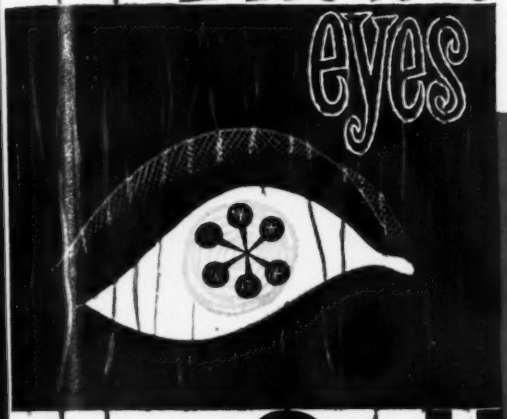

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FLINTKOTE COMPANY

Flintkote, a diversified building products company, maintains a substantial position in raw materials such as limestone, asbestos and timber. Chief interest lies in the company's plans to reach nationwide status in cement, gypsum and paper containers. Earnings this year are expected to be about $3.00 (adjusted for the 3 for 2 stock split.) These shares, selling at 13 times anticipated earnings, appear attractive for long-term growth.

For several years, Flintkote has been maneuvering to place itself in a strategic position in order to obtain major benefits from the high levels of construction expected in the 1960's, especially in residential building. For this reason, starting from a base in asphalt and asbestos cement building products, numerous mergers have been implemented by the new management. These have brought Flintkote into several new areas where the earnings and growth potentials are far greater than previously. In 1958, building products—roofing, siding, and building slabs, accounted for 33% of sales; paper containers 26%; asbestos products, chemical lime, cement, gypsum and aggregates 12%; floor coverings and adhesives, 12%; industrial products 9%, and pipe and conduit 8%. Generally speaking, profit margins on gypsum, asbestos, pipe and paper products have been higher than on floor coverings, roofing and industrial proudcts. At the moment the approval by the stockholders of the Glens Falls Portland Cement Company is awaited on a proposed merger. Last month Flintkote stockholders approved acquisition of the Blue Diamond Corporation, a $20 million California supplier of gypsum, ready-mixed concrete, and aggregates. In 1958, Orangeburg Manufacturing Company (pipe), Hankin Container Corp., Utah Lime Company, and a prefabricated chimney operation were acquired. Internally, Flintkote grew by completion of a gypsum plant in 1957 which has proved to be highly profitable, and expansion of cement and Insulrock (structural insulation) capacity in 1957-8.

Eventually the company's program envisages a nationwide position in cement, chemical lime (Flintkote is the largest chemical lime producer in the West) and gypsum. This would be in addition to the present broad geographic base in roofing, sidings and paper containers. Profitable opportunities in Insulrock, pipes, prefabricated chimneys and asbestos will also be exploited. Large size, of itself, facilitates growth, particularly through the greater financial strength afforded. There are management and control benefits also, since many operations are similar in that they involve the exploitation of raw materials—for example, limestone and asbestos. Merchandising on a national basis is aided through advertising efficiencies and the ability to better meet the needs of nationwide customers.

A study of the postwar financial history of the company supplies clues to the motivation for the expansion program. Starting with a heavy position in roofing and siding, earnings for many years failed to follow growth in volume, as margins weakened. Sales for 1952 were $84 million compared to $156 million last year. Again in 1952, common earnings were $2.41 compared to $1.98 in 1958 (adjusting for the 3/26/59 split). Depletion and depreciation jumped 107% in this period, which held back net earnings to

FLINTKOTE COMPANY

Price	$40
Dividend	$1.80 (1)
Yield	4.5%
1959 Price Range	40¾-38⅛
Traded	N.Y.S.E.

Capitalization (12/31/58)	
4⅜% Deb.	$10.0 million
3% Notes	2.6 million (2)
$4 cum. pfd.	60,555 shs.
4½% $100 Par 2nd pfd.	72,965 shs. (3)
$4.50 $100 par Series A 2nd pfd.	132,122 shs. (4)
Common	3,263,292 shs. (5)

(1) Indicated. (2) Since 12/58 $10.0 million revolving credit arranged. (3) Each share convertible to 3.1 common shares, adjusted for 3/59 split. (4) Conversion rate 1 common share each $37.334 par value adjusted for 3/59 split. (5) Outstanding after 3 for 2 split 3/26/59.

some extent. Taking 1957 to represent recent earning power would perhaps be more appropriate since early 1958 was unusually poor, the company reporting the only quarterly loss since World War II. Per share earnings in 1957 were $2.28.

Management expects a high level of earnings in 1959, with sales predicted in excess of $200 million. We believe the company will report net earnings of $3.00 or better. The year will be benefitted by recent expansion and acquisitions, higher prices for asphalt roofing in particular, and a generally high level for building. In the first quarter of 1959 earnings were 32¢ per common share compared to 5¢ (pro forma) in 1958. On June 15, 1959 the company intends to initiate a 45¢ quarterly dividend on the common, which represents a 5¢ rise in the rate of cash payments. At the time it was declared, the company stated that this was justified by the improved outlook.

ANACONDA CO.

Anaconda Company is one of the largest mining enterprises in the world. The company is a dominant factor in copper, one of the leading producers of zinc, and also turns out a long list of other metals, ranging from aluminum to uranium. It is also a major copper fabricator through its subsidiaries, including the wholly-owned American Brass Co. and the 70.7% owned Anaconda Wire & Cable Co. Anaconda produces some 15% of all the copper being mined in the world today, and its huge reserves comprise about 40% of all the world's known supply.

In 1958, Anaconda's mines produced 830 million pounds of copper, down from 902 million in 1957. Other production included 318 million pounds of zinc, 99 million pounds of aluminum, 44 million pounds of lead, 7.3 million ounces of silver, 59,000 ounces of gold, as well as manganese, ferro-manganese, arsenic, cadmium, phosphate and lumber. Output of virtually all the metals were less than in 1958 due to depressed demand, particularly early in the year.

In common with other metal producers, Anaconda's earnings dropped sharply in the past two years, falling from a peak of $10.40 a share in 1956 (adjusted to the present capitalization) to $4.23 in 1957 and to only $3.15 a share in 1958. However, it should be noted that with the upturn in copper which started in mid-1958, Anaconda's earnings began to recover briskly. Net in the third quarter of

ANACONDA CO.

Price	$66	Capitalization (12/31/58)	
Dividend	$2.00	Long-term debt	$95,5[illegible]6,000
Yield	3.0%	Common stock	10,714,6[illegible]7 shs.
1959 Price Range	74⅞-60⅛		
Traded	N.Y.S.E.		

last year climbed to 80¢ from the low of 43¢ touched in the second quarter. It then soared to $1.35 in the fourth quarter, the best three-month period since early 1957, and pushed still higher to $1.52 in 1959's opening quarter.

Barring any changes in metal prices or a long interruption in production or both, Anaconda seems capable of netting more than $6 in 1959. Moreover, we believe the chances of higher copper prices before the end of 1959 are strong, which would move Anaconda's earnings even higher. With producer inventories at a low level, fabricator business improving rapidly, and the general level of industrial activity soaring to new records, the copper market is likely to rise from the present 31½¢.

Furthermore, Anaconda's big new El Salvador mine in Chile is nearing completion. This will add to the company's capacity, even though the old Poterillos mine will be closed down. With the new mine fully broken in, we would estimate that Anaconda's basic earning power at 30¢ copper will rise to approximately $7 a share annually, with proportionately higher earning power displayed at higher copper prices. Given another year like 1956, when copper averaged more than 41¢ a pound (which was of course the highest level in almost a century) the company, including the new mine, would probably be capable of earning $13-$15 a share.

In view of the fact that copper prices are quite likely to move well above the present level some time in 1959-60, plus the likelihood that Anaconda's aluminum operations should start contributing to reported earnings for the first time in 1960, the shares seem reasonably priced for intermediate term application.◄

Esidrix-Serpasil *(Ciba)*

Each tablet contains 25 mg. of hydrochlorothiazide and 0.1 mg. of reserpine. *Indications:* In all grades of hypertension, particularly when one or more of the following symptoms coexists: Anxiety, tachycardia, congestive failure, swollen ankles, pitting edema, overweight edema, and other edematous conditions. *Dosage:* To be determined by the physician. *Supplied:* In bottles containing 100 tablets.

Florinef Ophthalmic Solution *(Squibb)*

Corticosteroid preparation, fludrocortisone hemisuccinate, in a sterile aqueous solution. *Indications:* For relief of itching, smarting or inflamed lesions of the eye. Reduces inflammation due to bacterial, allergenic or chemical agents, or foreign bodies. Inhibits ocular discharge and secretion. For acute conjunctivitis, vernal catarrh, chronic iridocyclitis and postoperatively in eye surgery. *Dosage:* One or 2 drops into the conjunctival sac 2 to 4 times daily. *Supplied:* In bottles containing 2.5 cc. of sterile aqueous solution.

Tigan *(Roche)*

Each capsule contains 100 mg. of medication. *Indications:* For prevention and treatment of nausea and vomiting. Useful in pregnancy, sickness due to land, air or sea travel, labyrinthitis, Meniere's syndrome, nausea and vomiting due to drugs, radiation therapy, infections and other diseases. May also be used for postoperative nausea and vomiting. *Dosage:* Recommended dose is 1 to 2 capsules every 4 hours, or as circumstances may require. *Supplied:* 100 mg. capsules.

Aristomin *(Lederle)*

Steroid-antihistamine compound. Each capsule contains 1 mg. of *Aristocort* (triamcinolone), 2 mg. of chlorpheniramine maleate and 75 mg. of ascorbic acid. *Indications:* For generalized pruritus, hay fever, allergic rhinitis, perennial asthma, seasonal and perennial rhinitis, vasomotor rhinitis, drug reactions and other manifestations of allergic sensitivity. *Dosage:* One to 8 capsules daily in divided doses, to be adjusted to patient's response. *Supplied:* In bottles containing 30 or 100 capsules.

ANACONDA CO.

Price	$66
Dividend	$2.00
Yield	3.0%
1959 Price Range	74⅞-60⅛
Traded	N.Y.S.E.

Capitalization (12/31/58)	
Long-term debt	$95,526,000
Common stock	10,714,627 shs.

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Dumogran *(Squibb)*

Oral therapeutic tissue-building preparation containing methyl-testosterone, ethinyl estradiol and vitamins and minerals. *Indications:* For relief of the clinical symptoms and after effects of the menopause. For use during and following the male climacteric. Restores muscle tone, promotes emotional balance, mental alertness in middle-aged and geriatric patients. *Dosage:* As directed by the physician. *Supplied:* In bottles containing 60 or 250 tablets.

Rautrax *(Squibb)*

Each tablet contains 50 mg. of whole root Rauwolfia Serpentina, 400 mg. of flumethiazide and 400 mg. of potassium chloride. *Indications:* For all degrees of hypertension. Affords reduction of elevated blood pressure and control of any associated edema. Lessens the need for rigid salt restriction, allowing a more palatable diet. *Dosage:* As directed by the physician. *Supplied:* In bottles of 100 capsule-shaped tablets.

Ionamin Capsules *(Strasenburgh)*

Non-amphetamine treatment for exogenous obesity. Available in two strengths: Each capsule contains either 15 or 30 mg. of phenyl-*tert.*-butylamine as a resin complex. *Indications:* For 10 to 14 hour appetite curb in obese patients, including those who are arthritic, diabetic, pregnant, menopausal, aged, and to reduce surgical risks. *Dosage:* One capsule daily. *Supplied:* Either strength, in bottles containing 100 or 400 capsules.

Alpha-Keri *(Westwood)*

Antipruritic oil containing a dewaxed, oil-soluble, keratin-moisturizing fraction of lanolin, with mineral oil and a nonionic emulsifier. *Indications:* To lubricate skin, relieve itching and restore the protective action of lost skin lipids. *Dosage:* For use in the bath, shower, or as a sponge bath. *Supplied:* In bottles containing 8 fluid ounces.

Theruhistin Forte *(Ayerst)*

New form. Antiallergic tablet with sustained action. Each tablet contains 24 mg. of isothipendyl hydrochloride. *Indications:* Sustained symptomatic relief of allergic disorders including tree, rose, and hay fever, vasomotor and allergic rhinitis, allergic dermatoses, drug allergies and food allergies. Also for relief of bronchial asthma. *Dosage:* One tablet morning and evening. *Supplied:* In bottles containing 100 or 1,000 tablets.

Tessalon Ampuls *(Ciba)*

New form. Cough control agent. Each 1 cc. ampul contains 5 mg. of benzonatate. *Indications:* For acute respiratory conditions: Bronchitis, pneumonia, common cold, upper respiratory infections, pleurisy, spontaneous pneumothorax, bronchial irritation provoked by gases and foreign bodies, measles, pertussis. *Dosage:* Intramuscularly or intravenously, as directed by the physician. *Supplied:* In 1 cc. ampuls, each containing 5 mg. of medication; cartons of 5.

The Incidence and Clinical Significance of Stainable Iron

The materials used in this study were bone marrow specimens obtained from 162 individuals: 21 normal subjects and 18 patients with no anemia, 37 patients with iron-deficiency anemia, 86 patients with a large variety of anemias, the main cause unrelated to iron deficiency.

Iron-deficiency anemia in 13 was due to acute massive hemorrhage, in 10 to chronic bleeding, and in 14 to hookworm infestation. The hemoglobin of this group was 3.0 to 11.0 gm., the lowest erythrocyte count 1,350,000. In three cases the counts were over four million. None had been treated with iron, at least for several weeks. Subsequent iron therapy produced good reticulocyte response and gradual improvement of anemia.

Three patients had megaloblastic anemia, seven hemolytic anemia, 30 chronic or subacute infections or sepsis. Some of the patients were given iron by mouth after the examination of the marrow, but neither reticulocyte response nor alleviation of anemia was observed unless the primary disease had been properly treated. The hemoglobin of this group was 1.0 to 11.5 gm., erythrocytes 500,000 to 3,870,000.

The bone marrow was aspirated either from the sternum or from the iliac crest. Some of the films were stained for iron directly, others with Wright's stain before staining for iron.

Not only the state of iron stores in the body, but also the capacity of the normoblasts to take up iron and utilize it for hemoglobin synthesis, are important factors that will influence the number of sideroblasts in the marrow and the character of the granules. In different types of anemia, the factors that will influence the intracorpuscular iron metabolism may also be different.

Bone marrow specimens of 162 normal and anemic subjects were studied with the Prussian blue stain. Extracellular hemosiderin and iron-containing granules in erythrocyte precursors were present in normal persons and also in anemic patients except in those with iron deficiency. The examination of extracellular hemosiderin and sideroblasts in the marrow provides a sensitive and reliable index of the availability of iron and is a useful adjunct for the study of iron metabolism. This simple method is valuable in the diagnosis of iron-deficiency anemia and serves as a guide for iron therapy. The percentage of sideroblasts in the marrow does not necessarily parallel the amount of extracellular hemosiderin. Simultaneous examination of both is therefore necessary for a better understanding of the iron metabolism in the body.

Chih-Fei, Y., *Chinese M.J.*, 77:347-355,1958.

Fostex®
treats their acne while they wash

degreases the skin helps remove blackheads dries and peels the skin

...and this is how it works

Fostex provides the essential actions necessary in treating acne. It washes off excess oil. It unblocks pores by penetrating and softening blackheads. It dries and peels the skin, removing papule coverings, thus permitting drainage of sebaceous glands.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions... enhanced by sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Your patients will like Fostex because it is so simple to use. They simply wash acne skin 2 to 4 times a day with Fostex, instead of using soap.

FOSTEX CREAM

... in 4.5 oz. jars. For therapeutic washing in the initial phase of oily acne treatment.

FOSTEX CAKE

... in bar form. For therapeutic washing to keep the skin dry and free of blackheads during maintenance therapy. Also used in relatively less oily acne.

Write for samples.

WESTWOOD PHARMACEUTICALS Buffalo 13, New York

Dietary Management of Hypercholesterolemia

Efforts are being made to gradually increase the use of foods rich in polyunsaturated fats while decreasing the intake of foods rich in saturated fats. Some now drink vegetable oil "cocktails" as part of their regular diet. The present study was carried out in a private hospital of 110 beds for the convalescent and the chronically ill. Sixty per cent of the patients had coronary heart disease and hypertension, 35% had suffered strokes, 20% showed senility. The average age of the 18 men and 87 women was 72 years. They represented a cross-section of cases at the hospital, with diagnoses of cardiovascular disease, hypertension, senility and diabetes, in that order of frequency.

The regular hospital diet was given for 30 days, with corn-oil margarine substituted for all solid fats. Changes in the blood cholesterol levels were determined after a return to the original diet. A total of seven cholesterol determinations for each patient was made over a 60-day period. Of the 190 persons who followed the dietary regimen, serum cholesterol levels were determined for only the 15 patients in this study. The patients accepted the test diet with as much spirit as the general hospital diet, and, apparently, without noticing the difference. Blood cholesterol samples were taken before breakfast and tests made within 24 hours, in duplicate. The average cholesterol on the general diet was 277 mg.%. At the end of the test diet it was 216 mg.%, an average reduction of 22%. Within 10 days after returning to the general hospital diet, in all but one of the patients the average cholesterol rise was 22%, to 265 mg.%. After 10 days more on the same diet, the figure was still 265 mg.%. There were no significant weight changes.

Terman, L. A., *Geriatrics*, 14:111-114,1959.

Amyotrophic Lateral Sclerosis

This uniformly fatal disease is one of weakness, atrophy, and fasciculation of muscles of the extremities and, less commonly, of the head. Other diseases in this category are progressive spinal muscular atrophy, primary lateral sclerosis, and progressive bulbar palsy. The incidence is four per 100,000 population in Europe and North America.

The age of onset in a series of 25 cases ranged from 26 to 68 years, average 51.6 years. Of 25 patients, 10 died, seven of respiratory failure. Fifty of 53 cases in a series showed involvement of the hypoglossal nuclei. Skeletal muscles showed atrophy of motor units. The onset is insidious. Fasciculations of muscle groups may be limited to the hands, face, tongue, or legs, or may be widespread from the beginning. In this study 12% were of the bulbar type.

Muscle atrophy is more common in the upper extremities. Weakness and wasting usually appear in the small muscles of the hands. The sensory system is very rarely affected. The psychiatric aspect has been studied.

Of the 23 cases available for follow-up, the longest duration was 66, the shortest 10 months. Death in most cases appears to be due to progression of bulbar symptoms. The clinical symptoms and findings include muscular atrophy, bulbar and pseudobulbar palsy and lateral sclerosis. The upper extremities were the most frequent site of onset.

Ladwig, H. A., et al., *Nebraska M.J.*, 44:18-25,1959.

In the Treatment of Rheumatic Disorders
Greater stability of maintenance dosage minimizes risks of hormonal imbalance

In Sterazolidin, the anti-inflammatory actions of prednisone and Butazoli are combined to permit lower effective dosage of each. Clinical experie has indicated that patients can be well maintained on this combination prolonged periods with relatively low, stable dosage levels of each compon thus minimizing the problems arising from excessively high doses of c costeroids. Other side effects have also been gratifyingly few. Antacid spasmolytic components are contained in Sterazolidin capsules for the be of patients with gastric sensitivity.

Sterazolidin®: Each capsule contains prednisone 1.25 mg.; phenylbuta 50 mg.; dried aluminum hydroxide gel 100 mg.; magnesium trisilicate 150 homatropine methylbromide 1.25 mg.

Detailed information available on request.

®Geigy's trademark for phenylbutazone—Reg. U. S. Pat. Off.

new **Sterazolidin®** Cape

prednisone-phenylbutazone, Geigy

Geigy Ardsley, New Y

Treatment of Lung Trauma

If the patient arrives in the emergency room conscious and in a fair condition, an orderly investigation can be made. In the great majority of cases, this is not the case, and a suggested routine is this:

The airway is immediately established by nasopharyngeal suction and the insertion of a Guedel oral airway. Nasal oxygen, six liters a minute, with a small plastic catheter, is begun only after the nasopharynx has been cleaned out. Meanwhile the physician investigates as to tension pneumothorax, hemothorax or hemopneumothorax. All that is required is a stethoscope, thumb and forefinger of one hand, good visual acuity, a good light and a naked thorax. If the patient has ashen cyanosis, dyspnea, grunting respirations, deviation of the trachea, chest lag or immobility, and hyperresonance and no breath sounds, tension pneumothorax is evident.

The skin of the affected side is prepared over the second anterior intercostal space, and a 15-guage needle with 3-way stopcock and a Luer-Lok syringe is inserted carefully until air can be withdrawn in 50 ml. increments until the emergency is somewhat less acute. The needle may also be connected via the stop-cock to a water-sealed drainage bottle. Observation of the underwater seal will soon indicate any massive air leak that may be due to lung rupture, or tracheal or bronchial trauma. If the bronchopleural fistula persists, an inter-rib catheter should be inserted in the second anterior intercostal space to expand the lung and maintain expansion. In adults it is better to use a 20 French fenestrated, soft-rubber catheter connected to a source of closed suction.

Pallid cyanosis, marked dyspnea or flat percussion note and progressive shock make hemothorax likely. Hemothorax may be minimal, but the sharp rib ends may lacerate an intercostal artery, which bleeds persistently, and demands immediate thoracentesis to aspirate all the blood possible and to re-expand the lung. This is repeated as indicated after replacement of blood volume. If a clotted hemothorax results, utilizing enzyme lysis may make surgical decortication unnecessary. If hemorrhage persists, a thoracotomy is mandatory.

Hemopneumothorax requires rapid expansion of the lung and ridding the pleural space of blood. If air leak continues, a 20 French catheter may be inserted through the second anterior intercostal space on the affected side, for two-thirds of its length, with many fenestrations to prevent obstruction by clots. The use of streptokinase-streptodornase may help with lysing of clot. If no expansion or clearing of the pleural space is evident after 18 hours, a thoracotomy must be considered.

Lane, W. Z., *New England J. Med.*, 260:251-255, 1959.

when fear-anxiety
finds its somatic outlet in
cardiac or g.i. symptoms[1]

SYCOTROL

1-piperidine ethanol benzilate hydrochloride

ANTIPHOBIC

without sedative or depressant effect

"...tends to abolish fears and resulting neurotic responses engendered by anxiety and stress. Discrimination and ego functions are not depressed."[1]

Dosage: 1 tablet, 3-4 times daily.

Supplied: 3 mg. tablets in bottles of 100.

Announcing

TWO NEW IMPORTANT MEDICATIONS

FOR THE PEPTIC ULCER TRIAD—
FEAR-ANXIETY, HYPERMOTILITY, HYPERACIDITY

THE
TRI-LOGISTIC
APPROACH

MODUTROL*

ANTIPHOBIC
ANTISPASMODIC
ANTACID

the presence of SYCOTROL—a specific for the fear-anxiety component—now makes possible total peptic ulcer therapy

Without rigid dietary restrictions, MODUTROL, as the sole medication, gave complete relief in previously resistant cases of peptic ulcer. No untoward side effects were seen even on prolonged therapy.[1]

*trademark

Formula: Each tablet contains: SYCOTROL 2 mg., propantheline methylsulfate 1 mg., magnesium hydroxide 200 mg., aluminum hydroxide 200 mg.

Dosage: 1 tablet q.i.d. or as determined by severity of the condition.

Supplied: Bottles of 50.

Reference: Greenblatt, L. A.: Clin. Med. 6:71, Jan. 1959.

REED & CARNRICK / JERSEY CITY 6, NEW JERSEY

Malignant Melanoma: Experience with 170 Cases

Thirty years ago a woman of 47 was seen with a large mass in the left axilla that was causing pressure symptoms. Some type of "mole" had been removed from the forearm a few months before. In an attempt to relieve her pain the axillary mass was removed, but thorough dissection was not carried out. She lived for 20 years and died of other causes. Perhaps melanomas are as curable as almost any other cancer.

In 30 years, case histories of 170 patients with this disease were collected—91 of them females. The ages were two to 84 years, the median age 47. Of these patients 48% had preexisting moles. It is generally believed that any mole subject to irritation from shoes or clothing, eyeglasses, razors and so forth should be removed.

Melanomas may reach the blood stream early and metastasize to distant parts of the body, may spread via the skin lymphatics or by emboli, through the deep lymphatics to lymph nodes. Some spread via blood *and* lymph. Removal of a strip of skin from the primary site to the drainage area should be removed for patients with known involvement of the skin lymphatics.

It is generally accepted that treatment of malignant melanoma is wide excision and radical removal of the lymph nodes in the area. It is not always possible to determine exactly the lymphatic spread, and so it may be wise to defer disscetion until nodes appear. Lesions of the extremities are particularly suitable for a unilateral regional dissection. Those of the head and neck may not metastasize at all, or may spread to nodes on both sides of the neck and require bilateral radical neck dissection.

It is suggested that palpation for lymph nodes is not an accurate method of finding metastases in such nodes and that, whenever possible, a regional lymph node dissection should be carried out.

Those continuing free of disease for five years after only a local excision numbered 55.5%.

The 5 year cure rate of all patients treated by local excision and regional dissection was 52.3%. When lymph nodes were negative, the rate was 71%; when nodes were positive, the rate was 26%.

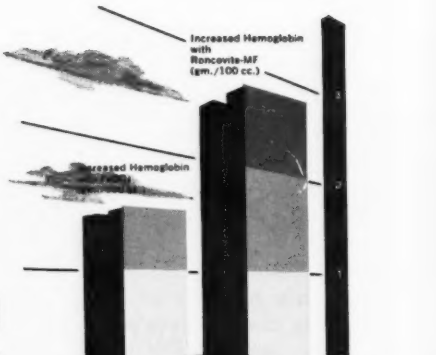
The 5 year cure rate when any attempt was made to eradicate the disease completely was 52.3%; only three patients had recurrences after five years. Nearly all patients who died of the disease did so within three years.

Precautionary regional dissection is considered of greatest value in lesions of the extremities. There were too few patients who did *not* undergo dissection for extremity lesions to give a parallel percentage of cures for the study. This study indicates that this disease can have a high cure rate if it is treated radically, and if the patients are followed carefully.

Daland, E. M., *New England J. Med.*, 260:453-460, 1959.

Operating Room Deaths

Fifty-nine deaths occurred in the operating rooms and recovery rooms at a large hospital in a recent 10-year period. There were 57,132 surgical procedures performed during this time. Of the 59 deaths, 51 (86%) occurred in the operating rooms, eight (14%) in the recovery room (in existence for half the 10-year period). Twelve per cent of the operations



Improved iron utilization in anemia

RONCOVITE®-mf

Each tablet contains: Cobalt chloride (Cobalt as Co....3.7 mg.)....15 mg. Ferrous sulfate, exsiccated....100 mg.

Improves iron utilization by enhancing the formation of erythropoietin, the erythropoietic hormone

Recent research[1,2] again emphasizes the role of cobalt as the only clinically proved agent which enhances erythropoietin formation.

The acceleration of erythropoiesis with Roncovite therapy provides optimal utilization of iron.

Acting through this physiologic mechanism, Roncovite (cobalt-iron) therapy results in an increased production of red cells and hemoglobin—a better blood picture—a faster, more complete response than iron alone in the common hypochromic anemias—menstrual anemia—anemia of pregnancy—nutritional anemia of infancy—and in anemia due to chronic infection or inflammation.[3,4,5,6,7,8]

(1) Goldwasser, E.; Jacobson, L. O.; Fried, W., and Pizak, L. F.: Blood 13:55 (Jan.) 1958. (2) Gurney, C. W.; Jacobson, L. O., and Goldwasser, E.: Ann. Int. Med. 49:363 (Aug.) 1958. (3) Korst, D. R.; Bishop, R. C., and Bothell, F. H.: J. Lab. & Clin. Med. 52:384 (Sept.) 1958. (4) Ausman, D. C.: Journal-Lancet 76:290 (Oct.) 1956. (5) Holly, R. G.: Obst. & Gynec. 9:299 (Mar.) 1957. (6) Holly, R. G.: Clin. Obst. & Gynec. 1:15 (Mar.) 1958. (7) Diamond, E. F.; Gonzales, F., and Pisani, A.: Illinois M. J. 113:154 (April) 1958. (8) Hill, J. M.; La Jous, J., and Sebastian, F. J.: Texas J. Med. 51:886 (Oct.) 1955.

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were done in emergency. Fifty-eight per cent of the deaths occurred during elective operations.

The death rate increased directly with the patients' age. Seventy-five per cent of the deaths occurred in patients whose operation took longer than one hour; 29% of all patients in this series were considered moribund; 75% of the deaths occurred in operations for new growths, perforated viscus due to disease and abnormality for repair or reconstruction. Ten of the 22 patients with new growths were very poor risks or moribund, and nine of them were in surgery for more than one hour. All of the patients with perforated viscus were very poor or moribund risks and all had operations lasting for more than one hour. Of the 15 patients operated upon for repair or reconstruction of an abnormality, 11 were very poor or moribund risks and six died during the first hour of anesthesia and operation. Twenty per cent of these deaths occurred during a reoperation.

Hemorrhage was a factor in 28 of the 59 deaths. Some of the patients were given blood for the treatment of shock other than that caused by hemorrhage.

Single anesthesia techniques were employed in 49 cases, combined techniques in 10. It was thought that death might possibly have been averted by better anesthesia management in 25% of the cases in which a single technique and in 75% of cases in which a combined technique was used.

Curare was used in seven per cent of all anesthetic administrations. The death rate was five times as high in the cases in which curare was used as in those in which it was not.

Shroff, P. F., *California Med.*, 90:9-13,1959.

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EATON LABORATORIES, NORWICH, NEW YORK

briefs: THERAPEUTIC

An Antibacterial Reduces Blood Pressure

The antibacterial nitrofuran (furazolidone) reduces high blood pressure, probably by interrupting various pathways of carbohydrate metabolism of tissues. In clinical trials of furazolidone on 16 patients, all diagnosed as having uncomplicated primary hypertension, the average reduction of mean arterial blood pressure was 39 mm. Hg., the time required for this response two to eight weeks. There is a gradual reduction to a stable plateau which cannot be lowered farther by increased doses, so orthostatic hypotension does not occur. The blood pressure of normotensives is unaltered. No restriction of salt or food intake was required. The dose of furazolidone was 800 mg. orally, this reduced gradually when the hypotensive response was stabilized. The reduced pressure could be maintained on as little as 200 mg. per day.

It is noted that certain nitrofurans have been shown to interrupt carbohydrate metabolism by inhibiting the anerobic formation of coenzyme A from pyruvate, and by impairing various enzymatic dehydrogenation systems. Furazolidone may also inhibit the conversion in vivo of acetaldehyde to acetate.

Metabolic studies showed that during furazolidone administration there was a decrease in total exchangeable sodium space and an increase in renal excretion of sodium, without alteration of serum sodium and potassium.

Calesnick, B., *Am. J.M. Sc.*, 236:736,1958.

Recent Advances in the Clinical Use of Radioactive Isotopes

Isotopes are elements that are similar chemically, have different atomic weights, and behave as do all other isotopes of that element. These elements are made radioactive by bombarding them with neutrons, or other high-energy particles, in a reactor or cyclotron. The techniques developed using radioactive isotopes, in the last 19 years, are put into three categories: tracers, isotope dilution, and activation.

By use of the Scintiscanner, we can depict the relative function of various portions of the thyroid gland and this scanner has aided determination of hepatic function in the same manner as in thyroid disease, that of giving a pictorial record. Radioactive rose bengal is injected intravenously and after a few minutes the Scintigram is made. The liver function is determined also by continuously measuring the uptake and subsequent excretion of the radioactive rose bengal by the liver.

Work is in progress to use both forms of chromium 51, thereby meas-

uring both plasma volume and red cell volume simultaneously. This should give a more accurate and rapid total blood volume determination. Previously, simultaneous injection of the chromate form of chromium 51 and iodinated albumin (RISA) have been used in this manner. Research is being carried out on laboratory animals in the hope of perfecting a method whereby blood volume determinations can be carried out continuously by the use of plastic coil within the scintillation well counter.

A technique which shows great promise is neutron activation analysis, a method by which infinitesimal amounts of trace elements within the body may be accurately determined. Many clinical diseases at this time are thought to be due to error in metabolism of specific elements. Examples are acrodynia (mercury), Wilson's disease (copper), and plumbism (lead).

The degree of accuracy of tracer and dilution techniques, using isotopes, has never before been available to the physician. As with other laboratory determinations, the interpretation of even such accurate findings must be made by close integration with the history and physical findings.

James, L. R., & Ogborn, R. E., *Nebraska M.J.*, 44: 72-76,1959.

Trace Elements in Cardiovascular Disease

Increased amounts of cadmium, lead and manganese are found in the urine of patients with malignant hypertension, suggesting that these metals may be present in hypertensive patients in adbnormally large amounts. When hypertensive patients are treated with agents such as hydralazine, the urinary levels of these metals drop toward normal. Excretion of vanadium is considerably less in hypertensive patients than in normal persons. Only after study of a large series of cases will it be possible to determine the role of metalloenzyme imbalances in arterial hypertension, and to apportion the contribution of each trace metal to that imbalance.

There exists an antagonism between copper and molybdenum in animal nutrition. Copper deficiency in cattle may be due to pasture grasses low in copper or high in molybdenum. A third factor enters, and perhaps a fourth: The degree of molybdenum suppression of copper depends upon the amount of inorganic sulfate in the diet, and the combined inhibitory effect of the molybdenum and the sulfate on copper utilization seems to depend upon the amount of manganese available. High manganese content will block the molybdenum-sulfate suppression of copper storage and utilization. Further, if the diet is very high in protein, manganese may augment rather than block the effects of molybdenum and sulfur on copper utilization.

For one trace metal, cobalt, the method of administration may be of significance. In cholesterol-fed rabbits and chickens, feeding of cobaltous chloride reduces the incidence and severity of aortic atheromatous lesions and lowers blood cholesterol concentrations. Parenterally administered cobalt, however, increases both the incidence and severity of aortic lesions and the level of cholesterol in the blood. This finding has important implications in therapy employing vitamin B_{12}.

Griffith, G., & Hegde, B., *Illinois M.J.*, 115:12-13, 1959.

Treatment in Hypertensive Crises

During the past decade, ability to control extreme blood pressure elevation has increased greatly. Continuous nursing supervision, frequent blood pressure determination, and use of vasopressor agents are requisites. Phenylephrine or metaraminol may be given intramuscularly. Before intravenous administration of a ganglionic blocking agent or of a veratrum extract, norepinephrine should be prepared for immediate use if needed. If shock occurs, the foot of the bed should be elevated on blocks to prevent cerebral ischemia and to encourage blood return to the heart.

Hypertensive crisis may occur in essential hypertension, toxemia of pregnancy, or acute glomerulonephritis. Before treatment, renal compensation should be appraised. If this is normal, renal failure is not responsible for any sensorial disturbance. If, during treatment, the level rises even though pressure is greatly reduced, norepinephrine should be given.

Retinal examination is also essential, since the severity of retinal hemorrhage indicates the degree of general arteriolar damage, and papilledema is suggestive of increased intracranial pressure and cerebral edema, with resultant deranged cerebral function in patients without renal failure.

Reserpine is the preferable drug when delay of two to three hours in pressure reduction is possible. If within this time response to initial dosage of 2.5. mg is inadequate, an additional 2.5 mg. may be given, and 5 mg. doses thereafter as needed. As much as 10 mg. per dose may be given. No more than 30 mg. should be given in 24 hours. Prolonged daily administration of more than 10 mg. depresses cerebration and may cause a Parkinson-like syndrome, these manifestations disappearing several days after the drug is discontinued.

When response to reserpine is inadequate or immediate pressure reduction is required, hexamethonium 10 mg. should be given parenterally. If not effective in an hour, subsequent 20 mg. doses are given according to pressure response. Bedrails should be used to prevent standing, which may result in syncope. Pressure is recorded every few minutes for a half-hour after injection. Such careful supervision is not necessary once effective dosage is determined. Tolerance usually requires increasing dosages. Amounts greater than 75 mg. rarely reduce pressure further, and increase the severity of side effects.

In hypertensive emergencies, 100 to 150 mg. of hexamethonium in 1,000 cc. of 5% glucose in distilled water is infused at a moderate rate until pressure begins to fall and is then adjusted, blood pressure and pulse rate determined every five minutes during the adjustment, then every 15 to 20 minutes. Ganglionic blocking agents are particularly useful in severe and acute heart failure in which pressure elevation is sudden.

Moyer, J. H., *Heart Bull.*, 8:16-17,1959.

Paralysis Agitans: Treatment with Chlorphenoxamine Hydrochloride

Of 161 patients with paralysis agitans ranging in age from 31 to 80, 53 per cent were improved with the administration of chlorphenoxamine hydrochloride, a derivative of diphen-

hydramine hydrochloride. The drug was shown to exert a more effective muscle relaxant activity than diphenhydhramine, and to stimulate and energize the patients without causing excitement or agitation. It was especially beneficial in patients suffering from visceral spasms. Some patients with frequency and urgency also benefited from its use. The muscle relaxant activity of the drug appeared gentle, since even in large doses there was no evidence of feebleness or flaccidity. Although the usual duration of effectiveness was four to six hours, a few patients were satisfactorily maintained on one tablet daily.

Improvement was observed in 15 of 29 patients with the postencephalic form of the disease, in 27 of 60 with the arteriosclerotic and in 43 of 72 with the idiopathic form. Favorable results were equally distributed among the age groups. Symptoms were controlled satisfactorily enough in 67 patients to discontinue previous medication, while it was found more advantageous to combine the drug with trihexyphenidyl in 30, with benzotropine methanesulfonate in 25, procyclidine in 12, ethoproprazine in 10 and diphenhydramine in 5. The 47 per cent not improved largely constituted patients with tremor as the predominant symptom or those in whom slight tremor was accentuated by the drug. Other side effects were minimal.

Doshay, L. J., & Constable, K., *J.A.M.A.*, 170:37-41,1959.

Carbon Monoxide Poisoning

For many years treatment for carbon monoxide poisoning has been inhalation of 7% carbon dioxide in oxygen (carbogen), which very greatly increases pulmonary ventilation and speeds clearance of carbon monoxide from the blood. The main life-saving application of this treatment is by first-aid workers, because severely poisoned patients will be dead or beyond recovery by the time they get to the hospital if carbogen treatment is not started by those who first reach them. In England carbogen was removed from ambulances and first-aid services several years ago on direction, privately circulated to authorities, of the Medical Research Council. Now, after nearly eight years, the Council has just issued a statement reversing its former advice and advocating restoration of carbogen, not 7%, but 5%.

When carbogen first displaced oxygen 40 years ago as the treatment for carbon-monoxide poisoning, it was used in 5% strength. Later it was found that 7% produced more vigorous breathing and so was more effective. In normal persons 7% carbogen doubled or trebled the pulmonary ventilation produced by 5% carbogen and increased the volume of respiration to seven times the amount when air or oxygen alone was breathed. A large-scale practical trial was carried out in New York by specially trained resuscitation crews over a period of eight years, during which 7,845 poisoned patients were treated. In the three years during which 5% carbogen was used in treating 2,854 patients, there were 234 deaths (82 per 1,000). In the next five years 7% carbogen was used for 4,991 patients, and 156 deaths occurred (31 per 1,000). Thus the deaths were reduced to one-third of what they would have been had 5% continued to be used.

Marriott, H. L., *Brit. M.J.*, 2:1591-1592,1958.

briefs: UROLOGICAL

Some Clinical Aspects of the Kidney Stone Problem

Urolithiasis is a recurrent disease in many persons, the rate varies from 15 to 20% for the common small calcium oxalate stone so often passed by individuals with an uninfected urine, to one as high as 60 to 70% for staghorn stones removed surgically from chronically infected kidneys. Despite an enormous amount of work, clinical and investigative, the cause of the great majority of urinary calculi is not known. Hyperparathyroidism is responsible for about 5% of the recurrent calcium-containing calculi and there are a few other conditions responsible for even fewer stones.

The usual chemical analysis of calculi has not been helpful. A new technique, crystallographic analysis, gives information of more value in treatment to prevent recurrence.

Certain general measures are applicable to all cases. The eradication of foci of infection, whether in the teeth, tonsils, prostate or elsewhere is indicated. Hyperparathyroidism must be ruled out. Faulty dietary habits should be corrected, a liberal fluid intake and regular adherence to the program assured. Stringent restrictions are unacceptable and unnecessary.

Prevention of uric acid and cystine tone formation depends on alkalinization of the urine. The best alkalinizer is sodium citrate; a mixture of potassium citrate and sodium citrate may be used in those on low-sodium diet. Three or four gm. three or four times daily in water in most cases will keep the pH at 7.5. This salt may be bought by the pound and used indefinitely without harm.

Prien, E. L., *J. Oklahoma M.A.*, 52:3-8,1959.

Hypertension with Unilateral Renal Dysfunction: Cure by Nephrectomy

Unilateral renal disease is, in some instances, hypertensive disease. Of all persons with hypertension less than two per cent have unilateral renal disease as a cause.

There are two groups:

1. That of renal artery disease, the recognition of which has been greatly augmented by the use of aortography.

2. Unilateral renal disease in which the only finding of significance is impaired function, the cause of which may often be morbid anatomy of obscure causation and varying little from normal.

Impaired function may be demonstrable by intravenous urography or may be normal, but excretion of PSP by one kidney may be reduced. Poor function of one kidney alone might be considered an indication for nephrectomy when there is asso-

ciated hypertensive vascular disease.

It would not be reasonable to subject all patients with hypertension to complete urological study in order to ferret out the few who may have unilateral renal disease. Intravenous urography should be a means of diagnosis of the hypertensive patient. If the hypertension is of recent onset and accelerated, and there is no cause apparent, differential renal studies are indicated. Disparity in renal size should suggest the possibility of unilateral renal disease, the smaller kidney being the initiator of the hypertensive process. The diagnosis established, nephrectomy should not be deferred.

Magnin, G. E., & Helland, N. J., *Wisconsin M.J.*, 58:107-110,1959.

Mortality Following Prostatectomy

Deaths following prostatic surgery at a large hospital were reviewed, comparing the years 1941 through 1946 with the years 1952 through 1956. The year 1945 was not included because of inadequate records. The mortality in the literature was reviewed, comparing the years 1940 through 1945 with the years 1950 through 1955; these two studies were then combined for final analysis.

In the first group, the 362 prostatectomies performed during 1941 through 1946 (1945 excluded), 291 were transurethral resections; 71 were open procedures suprapubic or perineal. Thirteen deaths followed the transurethral, seven deaths the open procedures.

From 1952 through 1956, 983 prostatectomies were performed, of which 798 were transurethral, 185 open procedures—suprapubic, retropubic or perineal. Seven deaths followed the transurethral; six deaths followed open operations. The mortality following transurethral resections in the earlier period was 4.4%, this decreased to 0.87% in the later period. There was also a similar drop in the mortality following open prostatectomy, from 9.9% to 3.2%.

Cardiac complications accounted for 30.3% of the deaths in 1941 to 1946, pyelonephritis with uremia for 19.5%, pneumonia for 13.3%, and pulmonary embolism for 7%. Perforation of the bladder and hemorrhage with shock caused 5.5% and 4.7% of the mortality, respectively.

During 1950 to 1955 cardiac complications caused 37.7% of the deaths, pulmonary embolism 21.3%, pneumonia 8.2%, carcinoma of the prostate 8.2%. Miscellaneous causes were carcinoma of the cecum and bladder, lower-nephron nephrosis, gastrointestinal hemorrhage, ileus, strangulated hernia, status epilepticus, and bladder necrosis.

Of the 13 deaths in the later group, 11 followed open prostatectomy, while 2 followed transurethral resection. It is believed that only by placing more emphasis on early ambulation following all types of prostatectomy will this cause of mortality be decreased. Avoidance of shock and depressing drugs reduced the incidence. The incidence of pulmonary embolism is less, and the fatality rate decidedly lower, when the Trendelenburg position and exercise are routinely used after the operation.

Only by a more thorough preoperative investigation of the patient, including the use of electrocardiograms and better postoperative care, can we further lower the mortality of prostatectomy.

Fox, P. G. Jr., et al., *North Carolina M.J.*, 20:67-69,1959.

BOOK REVIEWS

Tumors of the Lungs and Mediastium

by B. M. Fried, M.D., F.C.C.P., Montefiore Hospital. New York. Lea and Febiger, Philadelphia 6. 1958 $13.50

These tumors have been the main concern of the author for more than three decades since first stimulated by his discovery at autopsy of cancer of the lung in a patient who had died in a hospital for the tuberculous. Note is made that an article published as late as 1930 giving the high incidence of brain metastases from cancer of the lungs was questioned by so great an authority on malignant tumors as James Ewing. The book covers thoroughly every aspect of these tumors—histogenesis, etiology, clinical manifestations, metastatic manifestations, diagnostic procedures, and treatment by every means now available. A section is devoted to the rarer tumors of these organs and this region. Numbered among the contributing authors are a radiologist, a thoracic surgeon, and several internists. The subject is covered thoroughly, with no wastage of words, from a conservative viewpoint. Very appropriately the dedication is to Dr. Evarts A. Graham.

The Physical Treatment of Varicose Ulcers: A Practical Manual for the Physiotherapist and Nurse

by R. Rowden Foote, F.I.C.S., M.R.C.S., Surgeon-in-charge, Varicose Vein Clinic, Royal Waterloo Hospital for Women and Children, London. With a section on Electrical Adjuncts to Treatment by Miss T. Wareham, M.C.S.P. Superintendent Physiotherapist, St. Bartholomew's Hospital, London. E. & S. Livingstone, Ltd., Edinburgh and London. 1958. The Williams & Wilkins Company, Baltimore 2. $4.00

It is interesting to learn that this surgeon of large experience has found that "the majority of sufferers of varicose or venous ulcers can be made into useful, pain-free persons by the simplest of methods". Surgery, we are told, holds its place in the treatment of resistant cases and in the eradication of basic causes. Physiotherapy, compression treatment, and simple exercises, "will heal and keep healed the vast majority of ulcers".

If the book will supply information of how to accomplish even 50 per cent of this promise, no doctor could more wisely invest than in this book.

Surgical Pathology

by Lauren V. Ackerman, M.D., Washington University School of Medicine, in collaboration with Harvey R. Butcher, Jr. M.D., Washington University School of Medicine, St. Louis. With 1114 illustrations. Second edition. The C. V. Mosby Company, St. Louis 3. 1959. $15.00

Additions to this subject are being made daily by surgeons and pathologists all over the world. The first edition made judicious recordings of the status of surgical pathology of that time, and this second edition gives the same treatment to additions to knowledge in this field since the first edition was published. A book of this kind does not lend itself readily to critical review. It is almost entirely a statement of demonstrable facts, next to nothing of theory. There can be no doubt of the reliability of the factual statement, and the setting forth leaves nothing to be desired. The lucid text and ample illustrations make it a capital exposition of the subject for medical students and medical graduates.

Treatment in Internal Medicine

by Harold Thomas Hyman, M.D., Monmouth Memorial Hospital, Long Branch and Riverview Hospital, Red Bank, N.J. With foreword by Walter C. Alvarez, M.D. J. B. Lippincott Co., Philadelphia. 1958 $12.50

Dr. Alvarez says in his foreword that the author showed the medical world some years ago that he was a brilliant and able writer possessed of an encylopedic knowledge of the practice of medicine, and especially of therapeutics. The same discriminating authority said that Dr. Hyman's prose is interesting, crisp and readable, and that he has the gift of brevity. Of the present work, Dr. Alvarez says that Dr. Hyman has shown his ability to get out an immense book, and have each section on treatment up to date, with ample information on the practical use of drugs including those recently placed on the market. Nearly everybody in internal medicine knows Dr. Alvarez and is prepared to accept his judgement and act on it.

Therapeutic Radiology, Rationale, Technique, Results

by William T. Moss. M.D., Assistant Professor of Radiology, Northwestern University School of Medicine, Foreword by Lauren V. Ackerman, M.D. With 146 illustrations. The C. V. Mosby Company, St. Louis 3. 1959. $12.50

Against a sound the background of training in clinical medicine, the author has had a long training in radiotherapy in his own country and abroad, and had wide personal experience in the treatment of cancer by radiotherapeutic measures. It appears that radiotherapy to all organs and parts is covered expertly and in clear language. This reviewer can subscribe to the statement in the foreward that various specialists may find here that help which is so much needed in the care of their patients, and that it should be of very great value to the young physician begining a career in radiotherapy, and to the pathologist invaluable as a source of knowledge on the affects of irradiation on normal tissue.